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NEWS	2	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS	3	MAR 16	CASREACT coverage extended
NEWS	4	MAR 20	MARPAT now updated daily
NEWS	5	MAR 22	LWPI reloaded
NEWS	6	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS	7	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS	8	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS	9	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS	10	APR 30	CA/CAplus enhanced with 1870-1889 U.S. patent records
NEWS	11	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS	12	MAY 01	New CAS web site launched
NEWS	13	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS	14	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS	15	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS	16	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS	17	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS	18	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS	19	JUN 27	CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS	20	JUN 29	STN Viewer now available
NEWS	21	JUN 29	STN Express, Version 8.2, now available
NEWS	22	JUL 02	LEMBASE coverage updated
NEWS	23	JUL 02	LMEDLINE coverage updated
NEWS	24	JUL 02	SCISEARCH enhanced with complete author names
NEWS	25	JUL 02	CHEMCATS accession numbers revised
NEWS	26	JUL 02	CA/CAplus enhanced with utility model patents from China

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 4 MAY 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
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Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 09:45:37 ON 03 JUL 2007

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 09:45:58 ON 03 JUL 2007

FILE 'BIOSIS' ENTERED AT 09:45:58 ON 03 JUL 2007
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=> S Nephropathy
L1      108930 NEPHROPATHY

=> Dup Rem L1
108930 ANSWERS REQUESTED EXCEEDS MAXIMUM ALLOWED OF 50000
You may process up to 50,000 answers per command.  Please try to
narrow your search until your resulting L# answer set is within the
maximum number of answers.

=> S lysophosphatidic acid
L2       10068 LYSOPHOSPHATIDIC ACID

=> S EDG receptor
L3         419 EDG RECEPTOR

=> S L1 AND L2 AND L3
L4           0 L1 AND L2 AND L3

=> S L2 AND l3
L5         190 L2 AND L3

=> Dup Rem l5
PROCESSING COMPLETED FOR L5
L6          87 DUP REM L5 (103 DUPLICATES REMOVED)
               ANSWERS '1-39' FROM FILE MEDLINE
               ANSWERS '40-62' FROM FILE BIOSIS
               ANSWERS '63-82' FROM FILE CAPLUS
               ANSWERS '83-87' FROM FILE EMBASE

=> S L6 AND Therapy
L7           4 L6 AND THERAPY

=> D ti L7 1-4

L7   ANSWER 1 OF 4     MEDLINE on STN
TI   EDG receptors as a potential therapeutic target in
     retinal ischemia-reperfusion injury.

L7   ANSWER 2 OF 4     MEDLINE on STN
```

TI Critical role of lysophospholipids in the pathophysiology, diagnosis, and management of ovarian cancer.

L7 ANSWER 3 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI EDG receptors as a therapeutic target in retinal ischemic injury.

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lysophosphatidic acid is a bioactive mediator in ovarian cancer

=> D ibib abs L7 1-4

L7 ANSWER 1 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2006707700 MEDLINE
DOCUMENT NUMBER: PubMed ID: 17026968
TITLE: EDG receptors as a potential therapeutic target in retinal ischemia-reperfusion injury.
AUTHOR: Savitz Sean I; Dhallu Manjeet S; Malhotra Samit; Mammis Antonios; Ocava Lenore C; Rosenbaum Pearl S; Rosenbaum Daniel M
CORPORATE SOURCE: Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, USA.. drosenba@aecom.yu.edu
CONTRACT NUMBER: EY11257 (NEI)
EY1253 (NEI)
SOURCE: Brain research, (2006 Nov 6) Vol. 1118, No. 1, pp. 168-75. Electronic Publication: 2006-10-05.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200701
ENTRY DATE: Entered STN: 6 Dec 2006
Last Updated on STN: 24 Jan 2007
Entered Medline: 23 Jan 2007

AB LPA (lysophosphatidic acid) specific endothelial differentiation gene (EDG) receptors have been implicated in various anti-apoptotic pathways. Ischemia of the brain and retina causes neuronal apoptosis, which raises the possibility that EDG receptors participate in anti-apoptotic signaling in ischemic injury. We examined the expression of EDG receptors in a model of retinal ischemia-reperfusion injury and also tested LXR-1035, a novel analogue of LPA, in the rat following global retinal ischemic injury. Rats were subjected to 45 or 60 min of raised intraocular pressure. Animals were sacrificed at 24 h post-ischemia and retinal tissue was stained for EDG receptors. In separate experiments, animals were randomized to receive LXR or saline vehicle by intravitreal injection 24 h prior to ischemia. The degree of retinal damage was assessed morphologically by measuring the thickness of the inner retinal layers as well as functionally by electroretinography (ERG). We found that the normal retina has a baseline expression of the LPA receptors, EDG-2 and EDG-4, which are significantly upregulated in the inner layers in response to ischemia. Animals pretreated with LXR-1035 had dose-dependent, significant reductions in histopathologic damage and significant improvement in functional deficits compared with corresponding vehicle-controls, after 45 and 60 min of ischemia. These results suggest that LPA receptor signaling may play an important role in neuroprotection in retinal ischemia-reperfusion injury.

L7 ANSWER 2 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2002047383 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11775454
TITLE: Critical role of lysophospholipids in the pathophysiology, diagnosis, and management of ovarian cancer.
AUTHOR: Mills Gordon B; Eder Astrid; Fang Xianjun; Hasegawa Yutaka; Mao Muling; Lu Yiling; Tanyi Janos; Tabassam Fazal Haq; Wiener Jon; Lapushin Ruth; Yu Shiangxing; Parrott Jeff A; Compton Tim; Tribley Walter; Fishman David; Stack M Sharon; Gaudette Douglas; Jaffe Robert; Furui Tatsuro; Aoki Junken; Erickson James R
CORPORATE SOURCE: Department of Molecular Therapeutics, MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030, USA.
CONTRACT NUMBER: P01 CA64602 (NCI)
SOURCE: Cancer treatment and research, (2002) Vol. 107, pp. 259-83. Ref: 89
Journal code: 8008541. ISSN: 0927-3042.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 25 Jan 2002
Last Updated on STN: 24 Apr 2002
Entered Medline: 23 Apr 2002

AB Lysophosphatidic acid (LPA), the simplest of all phospholipids, exhibits pleiomorphic functions in multiple cell lineages. The effects of LPA appear to be mediated by binding of LPA to specific members of the endothelial differentiation gene (Edg) family of G protein-coupled receptors (GPCR). Edg 2, Edg4, and Edg7 are high affinity receptors for LPA, and Edg1 may be a low affinity receptor for LPA. PSP24 has been shown to be responsive to LPA in Xenopus oocytes, however, its role in mammalian cells is unclear. The specific biochemical events initiated by the different Edg receptors, as well as the biological outcomes of activation of the individual receptors, are only beginning to be determined. LPA levels are consistently elevated in the plasma and ascites of ovarian cancer patients, but not in most other epithelial tumors, with the exception of cervix and endometrium, suggesting that LPA may be of particular importance in the pathophysiology of ovarian cancer. In support of this concept, ovarian cancer cells constitutively and inducibly produce high levels of LPA and demonstrate markedly different responses to LPA than normal ovarian surface epithelium. Edg4 and Edg7 levels are consistently increased in malignant ovarian epithelial cells contributing to the aberrant response of ovarian cancer cells to LPA. Edg2 may represent a negative regulatory LPA receptor inducing apoptosis in ovarian cancer cells. Thus, increased levels of LPA, altered receptor expression and altered responses to LPA may contribute to the initiation, progression or outcome of ovarian cancer. Over 40% of known drugs target GPCR, making LPA receptors attractive targets for molecular therapeutics. Indeed, using the structure-function relationship of LPA in model systems, we have identified selective Edg2 anatgonists, as well as Edg4 and Edg7 agonists. These lead compounds are being assessed in preclinical model systems. Understanding the mechanisms regulating LPA production, metabolism and function could lead to improved methods for early detection and to new targets for therapy in ovarian cancer.

L7 ANSWER 3 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:47950 BIOSIS
DOCUMENT NUMBER: PREV200600057152
TITLE: EDG receptors as a therapeutic target in retinal ischemic injury.
AUTHOR(S): Rosenbaum, D. M. [Reprint Author]; Singh, M.; Malhotra, S.; Savitz, S. I.; Ocava, L. C.; Rosenbaum, P. S.
SOURCE: IOVS, (2005) Vol. 46, No. Suppl. S, pp. 5316. Meeting Info.: Annual Meeting of the Association-for-Research-in-Vision-and-Ophthalmology. Ft Lauderdale, FL, USA. May 01 -05, 2005. Assoc Res Vis & Ophthalmol. CODEN: IOVSDA. ISSN: 0146-0404.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jan 2006
Last Updated on STN: 4 Jan 2006

AB Purpose: EDG receptors are a family of G-protein coupled receptors that play an important role in cell growth, development and maintenance, survival and cytoskeletal changes. They exert their effect via intracellular signaling pathways involving various kinases. The purpose of this study was to evaluate the role of lysophosphatidic acid (LPA) -specific EDG receptors (EDG-2 and EDG-4) as therapeutic targets in a model of retinal ischemia. Methods: Transient retinalischemia was induced in Sprague-Dawley rats by increasing the intraocular pressure above systolic arterial pressure(HIOP) for 45 minutes. Immunohistochemistry for EDG receptor was performed at different times following reperfusion. In a separate set of experiments, intravitreal injections of a novel analog of LPA, LXR 1035, was given 6 hours before and 5 minutes after ischemia (HIOP). These animals were sacrificed at 7 days and retinal tissue harvested to evaluate retinal thickness and cell counts. Retinal function was evaluated by electroretinograms (ERG's). Results: EDG-2 and EDG-4 receptor staining was maximally evident at 24 hours following ischemia in the ganglion cell layer and the inner nuclear layer as compared to the sham group of animals where no staining was noted. The LXR 1035-treated group of animals showed significant preservation of retinal thickness, cell counts and retinal function as compared to the vehicle-treated group of animals. Conclusions: The neuroprotective effect of EDGreceptors in retinal ischemia-reperfusion maybe mediated via activation of phosphatidylinositol 3-kinase, Akt and MAPK and inhibiting cyclic AMP production. Therapies aimed at manipulating these receptors offers potential targets fortherapeutic strategies for ischemic retinal disorders.

L7 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:459270 CAPLUS
DOCUMENT NUMBER: 137:199096
TITLE: Lysophosphatidic acid is a bioactive mediator in ovarian cancer
AUTHOR(S): Fang, Xianjun; Schummer, Michel; Mao, Muling; Yu, Shuangxing; Tabassam, Fazal Haq; Swaby, Ramona; Hasegawa, Yutaka; Tanyi, Janos L.; LaPushin, Ruthie; Eder, Astrid; Jaffe, Robert; Erickson, Jim; Mills, Gordon B.
CORPORATE SOURCE: Department of Molecular Therapeutics, University of Texas M.D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Biochimica et Biophysica Acta, Molecular and Cell Biology of Lipids (2002), 1582(1-3), 257-264
CODEN: BBMLFG; ISSN: 1388-1981
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English
AB A review. Lysophosphatidic acid (LPA) is a naturally occurring phospholipid that exhibits pleiotrophic biol. activities, ranging from rapid morphol. changes to long-term cellular effects such as induction of gene expression and stimulation of cell proliferation and survival on a wide spectrum of cell types. LPA binds and activates distinct members of the Edg/LP subfamily of G protein-coupled receptors that link to multiple G proteins including G(i), G(q) and G(12/13) to elicit cellular responses. LPA plays a critical role as a general growth, survival and pro-angiogenic factor, in the regulation of physiol. and pathophysiol. processes in vivo and in vitro. Our previous work indicates that abnormalities in LPA metabolism and function in ovarian cancer patients may contribute to the initiation and progression of the disease. Thus, LPA could be a potential target for cancer therapy. This review summarizes evidence that implicates LPA in the pathophysiol. of human ovarian cancer and likely other types of human malignancies.
REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'BIOSIS' ENTERED AT 11:08:04 ON 03 JUL 2007
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.78	-0.78

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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 09:45:58 ON 03 JUL 2007
L1 108930 S NEPHROPATHY
L2 10068 S LYSOPHOSPHATIDIC ACID
L3 419 S EDG RECEPTOR
L4 0 S L1 AND L2 AND L3

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L5          190 S L2 AND L3
L6           87 DUP REM L5 (103 DUPLICATES REMOVED)
L7            4 S L6 AND THERAPY

=> S L6 AND modulator
L8            4 L6 AND MODULATOR

=> D Ti L8 1-4

L8   ANSWER 1 OF 4     MEDLINE on STN
TI   Native and recombinant human Edg4 receptor-mediated Ca(2+) signalling.

L8   ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Screening for substituted aryl isoxazole effectors of the Edg-1 receptor
     for the treatment of receptor-associated conditions

L8   ANSWER 3 OF 4  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Modulators of EDG receptors, LPA receptors,
     and S1P receptors for the modulation of neural stem cells and neural
     progenitor cells and treatment of nervous system disorders

L8   ANSWER 4 OF 4  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Methods using Edg receptor modulators for
     the treatment of Edg receptor-associated conditions


=> D Ibib Abs 1-4

L8   ANSWER 1 OF 4     MEDLINE on STN
ACCESSION NUMBER:   2004193628     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 15090154
TITLE:              Native and recombinant human Edg4 receptor-mediated Ca(2+)
                    signalling.
AUTHOR:             Simpson Peter B; Villullas Israel Ramos; Schurov Irina;
                    Kerby Julie; Millard Rachel; Haldon Christine; Beer
                    Margaret S; McAllister George
CORPORATE SOURCE:   Merck Sharp & Dohme Research Laboratories, Neuroscience
                    Research Centre, Harlow, Essex, UK..
                    peter_simpson@merck.com
SOURCE:             Assay and drug development technologies, (2002 Nov) Vol. 1,
                    No. 1 Pt 1, pp. 31-40.
                    Journal code: 101151468. ISSN: 1540-658X.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200405
ENTRY DATE:         Entered STN: 20 Apr 2004
                    Last Updated on STN: 20 May 2004
                    Entered Medline: 19 May 2004
AB   We have developed an assay system suitable for assessment of compound
     action on the Edg4 subtype of the widely expressed
     lysophosphatidic acid (LPA)-responsive Edg
     receptor family.  Edg4 was stably overexpressed in the rat
     hepatoma cell line Rh 7777, and a Ca(2+)-based FLIPR assay developed for
     measurement of functional responses.  In order to investigate the
     mechanisms linking Edg4 activation to cytosolic Ca(2+) elevation, we have
     also studied LPA signalling in a human neuroblastoma cell line that
     endogenously expresses Edg4.  LPA responses displayed similar kinetics and
     potency in the two cell lines.  The Ca(2+) signal generated by activation
     of LPA-sensitive receptors in these cells is mediated primarily by
     endoplasmic reticulum.  However, there is a substantial inhibition of the
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LPA response by FCCP, indicating that mitochondria also play a key role in the LPA response. Partial inhibition of the response by cyclosporin A could indicate an active Ca(2+) release role for mitochondria in the LPA response. The inositol 1,4,5-triphosphate receptor antagonist 2-aminoethyl diphenyl borate markedly inhibits, but does not abolish, the Ca(2+) response to LPA, suggesting further complexity to the signalling pathways activated by Edg receptors. In comparing Edg signalling in recombinant and native cells, there is a striking overall similarity in receptor expression pattern, agonist potency, and the effect of modulators on the Ca(2+) response. This indicates that the Edg4-overexpressing Rh7777 cell line is a very useful model system for studying receptor pharmacology and signalling mechanisms, and for investigating the Edg4 receptor's downstream effects.

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:80878 CAPLUS
DOCUMENT NUMBER: 140:139547
TITLE: Screening for substituted aryl isoxazole effectors of the Edg-1 receptor for the treatment of receptor-associated conditions
INVENTOR(S): Solow-Cordero, David; Shankar, Geetha; Gluchowski, Charles; Spencer, Juliet V.
PATENT ASSIGNEE(S): Ceretek Llc, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009816	A1	20040129	WO 2003-US22463	20030717
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2466288	A1	20040129	CA 2003-2466288	20030717
AU 2003252023	A1	20040209	AU 2003-252023	20030717
US 2004147562	A1	20040729	US 2003-621966	20030717
EP 1523556	A1	20050420	EP 2003-765716	20030717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005533852	T	20051110	JP 2004-523557	20030717

PRIORITY APPLN. INFO.:			
US 2002-397299P	P	20020718	
WO 2003-US22463	W	20030717	

OTHER SOURCE(S): MARPAT 140:139547
AB In one aspect, the present invention provides a method of modulating an Edg-1 receptor mediated biol. activity in a cell. A cell expressing the Edg-1 receptor is contacted with a modulator of the Edg-1 receptor sufficient to modulate the Edg-1 receptor mediated biol. activity. In another aspect, the present invention provides a method for modulating an Edg-1 receptor mediated biol. activity in a subject. A therapeutically effective amount of a modulator of the Edg-1 receptor is administered to the subject.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:913038 CAPLUS
DOCUMENT NUMBER: 139:375041
TITLE: Modulators of EDG receptors, LPA receptors, and S1P receptors for the modulation of neural stem cells and neural progenitor cells and treatment of nervous system disorders
INVENTOR(S): Lindquist, Per; Mercer, Alex; Ronnholm, Harriet; Wikstrom, Lilian
PATENT ASSIGNEE(S): Neuronova A.B., Swed.
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003094965	A2	20031120	WO 2003-IB2370		20030508
WO 2003094965	A3	20040722			
WO 2003094965	A8	20040826			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2003233119	A1	20031111	AU 2003-233119		20030508
US 2004014662	A1	20040122	US 2003-434943		20030508
PRIORITY APPLN. INFO.:			US 2002-379114P	P	20020508
			US 2002-393159P	P	20020702
			WO 2003-IB2370	W	20030508

AB The invention discloses methods of influencing central nervous system cells to produce progeny useful in the treatment of CNS disorders. More specifically, the invention includes methods of exposing a patient suffering from such a disorder to a reagent that modulates the proliferation, migration, differentiation and survival of central nervous system cells via sphingosine-1-phosphate (S1P) or lysophosphatidic acid (LPA) signaling. These methods are useful for reducing at least one symptom of the disorder. The methodol. of the invention uses modulators of S1P, LPA, or EDG receptors.

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:591307 CAPLUS
DOCUMENT NUMBER: 139:143997
TITLE: Methods using Edg receptor modulators for the treatment of Edg receptor-associated conditions
INVENTOR(S): Shankar, Geetha; Solow-Cordero, David; Spencer, Juliet V.; Gluchowski, Charles
PATENT ASSIGNEE(S): Ceretek LLC, USA
SOURCE: PCT Int. Appl., 293 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062392	A2	20030731	WO 2003-US1881	20030121
WO 2003062392	A3	20050120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
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CA 2473740	A1	20030731	CA 2003-2473740	20030121
AU 2003214873	A1	20030902	AU 2003-214873	20030121
EP 1513522	A2	20050316	EP 2003-710713	20030121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005519915	T	20050707	JP 2003-562260	20030121
US 2005261298	A1	20051124	US 2003-390428	20030314
PRIORITY APPLN. INFO.:			US 2002-350445P	P 20020118
			US 2002-350446P	P 20020118
			US 2002-350447P	P 20020118
			US 2002-350448P	P 20020118
			WO 2003-US1881	W 20030121
			US 2003-352579	B2 20030127

OTHER SOURCE(S): MARPAT 139:143997

AB The invention provides a method of modulating an Edg-2, Edg-3, Ed-4 or Edg7 receptor-mediated biol. activity in a cell. A cell expressing the Edg-2, Edg-3, Edg-4 or Edg 7 receptor is contacted with a modulator of the Edg-2, Edg-3, Ed-4 or Edg 7 receptor sufficient to modulate receptor mediated biol. activity. In another aspect, the present invention provides a method for modulating an Edg-2, Edg-3, Ed-4 or Edg-7 receptor mediated biol. in a subject. A therapeutically effective amount of a modulator of the Edg-2, Edg-3, Ed-4 or Edg7 receptor is administered to the subject. Preparation of compds., e.g. 4,4,4-trifluoro-3-oxo-N-(5-phenyl-2H-pyrazol-3-yl)butyramide, is described.

=> D Hist

(FILE 'HOME' ENTERED AT 09:45:37 ON 03 JUL 2007)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 09:45:58 ON 03 JUL 2007
L1 108930 S NEPHROPATHY
L2 10068 S LYSOPHOSPHATIDIC ACID
L3 419 S EDG RECEPTOR
L4 0 S L1 AND L2 AND L3
L5 190 S L2 AND L3
L6 87 DUP REM L5 (103 DUPLICATES REMOVED)
L7 4 S L6 AND THERAPY
L8 4 S L6 AND MODULATOR

=> S L2 (S)(agonist OR Analog OR antagonist OR Inhibitor)
L9 1072 L2 (S)(AGONIST OR ANALOG OR ANTAGONIST OR INHIBITOR)

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=> S L9 AND pd<=20031211
   2 FILES SEARCHED...
L10         695 L9 AND PD<=20031211

=> Dup rem L10
PROCESSING COMPLETED FOR L10
L11         303 DUP REM L10 (392 DUPLICATES REMOVED)
                ANSWERS '1-144' FROM FILE MEDLINE
                ANSWERS '145-200' FROM FILE BIOSIS
                ANSWERS '201-292' FROM FILE CAPLUS
                ANSWERS '293-303' FROM FILE EMBASE

=> S L11 (S)(EDG-2 OR EDG2 OR LPA1)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L56 (S)(EDG-2'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L58 (S)(EDG-2'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L60 (S)(EDG-2'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L62 (S)(EDG-2'
L12          37 L11 (S)(EDG-2 OR EDG2 OR LPA1)

=> D ti L12 1-37

L12  ANSWER 1 OF 37     MEDLINE on STN
TI   Cyclic phosphatidic acid elicits neurotrophin-like actions in embryonic
     hippocampal neurons.

L12  ANSWER 2 OF 37     MEDLINE on STN
TI   Pharmacological characterization of lysophospholipid receptor signal
     transduction pathways in rat cerebrocortical astrocytes.

L12  ANSWER 3 OF 37     MEDLINE on STN
TI   Ki16425, a subtype-selective antagonist for EDG-family
     lysophosphatidic acid receptors.

L12  ANSWER 4 OF 37     MEDLINE on STN
TI   Subtype-selective antagonists of lysophosphatidic
     Acid receptors inhibit platelet activation triggered by the lipid
     core of atherosclerotic plaques.

L12  ANSWER 5 OF 37     MEDLINE on STN
TI   Agonist-induced endocytosis of lysophosphatidic
     acid-coupled LPA1/EDG-2 receptors
     via a dynamin2- and Rab5-dependent pathway.

L12  ANSWER 6 OF 37     MEDLINE on STN
TI   Human platelets respond differentially to lysophosphatidic acids having a
     highly unsaturated fatty acyl group and alkyl ether-linked
     lysophosphatidic acids.

L12  ANSWER 7 OF 37     MEDLINE on STN
TI   Molecular basis for lysophosphatidic acid receptor
     antagonist selectivity.

L12  ANSWER 8 OF 37     MEDLINE on STN
TI   Noradrenaline release-inhibiting receptors on PC12 cells devoid of
     alpha(2(-)) and CB(1) receptors: similarities to presynaptic imidazoline
     and edg receptors.

L12  ANSWER 9 OF 37     MEDLINE on STN
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TI Activity of 2-substituted lysophosphatidic acid (LPA) analogs at LPA receptors: discovery of a LPA1/LPA3 receptor antagonist.

L12 ANSWER 10 OF 37 MEDLINE on STN
TI Identification of lysophospholipid receptors in human platelets: the relation of two agonists, lysophosphatidic acid and sphingosine 1-phosphate.

L12 ANSWER 11 OF 37 MEDLINE on STN
TI Naturally occurring analogs of lysophosphatidic acid elicit different cellular responses through selective activation of multiple receptor subtypes.

L12 ANSWER 12 OF 37 MEDLINE on STN
TI Edg-2/Vzg-1 couples to the yeast pheromone response pathway selectively in response to lysophosphatidic acid.

L12 ANSWER 13 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Lack of stereospecificity in lysophosphatidic acid enantiomer-induced calcium mobilization in human erythroleukemia cells.

L12 ANSWER 14 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI LYSOPHOSPHATIDIC ACID IS A GROWTH FACTOR FOR HEPATIC OVAL (STEM) CELLS.

L12 ANSWER 15 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI CHARACTERIZATION OF LYSOPHOSPHOLIPID RECEPTOR (LPR) SIGNAL TRANSDUCTION PATHWAYS IN RAT CORTICAL ASTROCYTES (AST).

L12 ANSWER 16 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Lysophosphatidic acid (LPA) regulation of murine blastocyst development involves crosstalk with embryonic heparin-binding epidermal growth factor-like growth factor (HB-EGF).

L12 ANSWER 17 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Fatty alcohol phosphates are subtype-selective agonists and antagonists of lysophosphatidic acid receptors.

L12 ANSWER 18 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI A dual lysophosphatidic acid (LPA) antagonist (LPA1/LPA3), VPC 12249, reduces renal ischemia-reperfusion injury (IRI).

L12 ANSWER 19 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Stereochemical properties of lysophosphatidic acid receptor activation and metabolism.

L12 ANSWER 20 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Lysophosphatidic acid (LPA) induced hypertrophy in rat neonatal myocytes.

L12 ANSWER 21 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI LPA analogs as agonists of the Edg2 LPA receptor.

L12 ANSWER 22 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Agonist-induced internalization of lysophosphatidic acid-coupled Edg2 receptors via clathrin-dependent endocytosis.

L12 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of N-(2'-carbamoyl-1,1'-biphenyl-2-ylcarbonyl)-β-alanine derivatives as lysophosphatidic acid receptor antagonists

L12 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lysophosphatidic acid (LPA) receptor agonists and antagonists, their preparation, and methods of use

L12 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Identification of p2y9/GPR23 as a Novel G Protein-coupled Receptor for Lysophosphatidic Acid, Structurally Distant from the Edg Family

L12 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lysophosphatidic acid (LPA) receptor agonists and antagonists, their preparation, and methods of use

L12 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Synthesis and biological evaluation of lysophosphatidic acid antagonists

L12 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Molecular modeling of lysophosphatidic acid receptor antagonists

L12 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Novel lysophosphatidic acid receptor agonists and antagonists

L12 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Role of ether-linked lysophosphatidic acids in ovarian cancer cells

L12 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Synthesis of lysophosphatidic acid receptor agonists and antagonists and their use for cancer inhibition, wound healing, and enhancement of cell proliferation

L12 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Assessment of agonism at G-protein coupled receptors by phosphatidic acid and lysophosphatidic acid in human embryonic kidney 293 cells

L12 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Methods for detecting compounds which modulate the activity of LPA (lysophosphatidic acid) and its receptor EDG-2

L12 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lysophosphatidic acid (LPA) receptors of the EDG family are differentially activated by LPA species. Structure-activity relationship of cloned LPA receptors

L12 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
TI Analysis of the EDG2 receptor based on the structure/activity relationship of LPA

L12 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

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TI   Methods using a lysophosphatidic acid receptor
     agonist for promoting survival of myelin-producing cells

L12  ANSWER 37 OF 37  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Recombinant human G protein-coupled lysophosphatidic acid receptors
     mediate intracellular calcium mobilization


=> Log off H
 SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 11:17:22 ON 03 JUL 2007

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PASSWORD:
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FILE 'MEDLINE' ENTERED AT 11:22:07 ON 03 JUL 2007
FILE 'BIOSIS' ENTERED AT 11:22:07 ON 03 JUL 2007
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FILE 'EMBASE' ENTERED AT 11:22:07 ON 03 JUL 2007
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FULL ESTIMATED COST                                69.83      70.04

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                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                -3.12      -3.12

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     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 09:45:58 ON 03 JUL 2007
L1       108930 S NEPHROPATHY
L2        10068 S LYSOPHOSPHATIDIC ACID
L3          419 S EDG RECEPTOR
L4            0 S L1 AND L2 AND L3
L5          190 S L2 AND L3
L6           87 DUP REM L5 (103 DUPLICATES REMOVED)
L7            4 S L6 AND THERAPY
L8            4 S L6 AND MODULATOR
L9         1072 S L2 (S)(AGONIST OR ANALOG OR ANTAGONIST OR INHIBITOR)
L10         695 S L9 AND PD<=20031211
L11         303 DUP REM L10 (392 DUPLICATES REMOVED)
L12          37 S L11 (S)(EDG-2 OR EDG2 OR LPA1)

=> D Ibib Abs L12 18

L12  ANSWER 18 OF 37  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on
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STN
ACCESSION NUMBER: 2002:567555 BIOSIS
DOCUMENT NUMBER: PREV200200567555
TITLE: A dual lysophosphatidic acid (LPA) antagonist (LPA1/LPA3), VPC 12249, reduces renal ischemia-reperfusion injury (IRI).
AUTHOR(S): Okusa, Mark D. [Reprint author]; Ye, Hong [Reprint author]; Huang, Liping [Reprint author]; Heise, Christopher E.; Santos, Webster L.; MacDonald, Timonthy; Lynch, Kevin R.
CORPORATE SOURCE: Medicine, University of Virginia, Charlottesville, VA, USA
SOURCE: Journal of the American Society of Nephrology, (September, 2002) Vol. 13, No. Program and Abstracts Issue, pp. 140A. print.
Meeting Info.: Meeting of the American Society of Nephrology. Philadelphia, PA, USA. October 30-November 04, 2002. American Society of Nephrology.
CODEN: JASNEU. ISSN: 1046-6673.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2002
Last Updated on STN: 7 Nov 2002

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	74.35	74.56
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.12	-3.12

FILE 'STNGUIDE' ENTERED AT 11:23:39 ON 03 JUL 2007
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Jun 29, 2007 (20070629/UP).

=> D Ibib ABS L12 11, 17,21-24,26,27,29,31,32
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L12 ANSWER 11 OF 37 MEDLINE on STN
ACCESSION NUMBER: 1999074344 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9855625
TITLE: Naturally occurring analogs of lysophosphatidic acid elicit different cellular responses through selective activation of multiple receptor subtypes.
AUTHOR: Fischer D J; Liliom K; Guo Z; Nusser N; Virag T; Murakami-Murofushi K; Kobayashi S; Erickson J R; Sun G; Miller D D; Tigyi G
CORPORATE SOURCE: Department of Physiology and Biophysics, The University of Tennessee, Memphis, TN 38163, USA.
CONTRACT NUMBER: HL07746 (NHLBI)
SOURCE: Molecular pharmacology, (1998 Dec) Vol. 54, No. 6, pp. 979-88.
Journal code: 0035623. ISSN: 0026-895X.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 28 Jan 1999
Last Updated on STN: 28 Jan 1999
Entered Medline: 12 Jan 1999

AB Lysophosphatidic acid (LPA), plasmalogen-glycerophosphate (alkenyl-GP) and, cyclic-phosphatidic acid (cyclic-PA) are naturally occurring phospholipid growth factors (PLGFs). PLGFs elicit diverse biological effects via the activation of G protein-coupled receptors in a variety of cell types. In NIH3T3 fibroblasts, LPA and alkenyl-GP both induced proliferation, whereas cyclic-PA was antiproliferative. LPA and alkenyl-GP decreased cAMP in a pertussis toxin-sensitive manner, whereas cyclic-PA caused cAMP to increase. LPA and alkenyl-GP both stimulated the activity of the mitogen-actived protein kinases extracellular signal regulated kinases 1 and 2 and c-Jun NH2-terminal kinase, whereas cyclic-PA did not. All three PLGFs induced the formation of stress fibers in NIH3T3 fibroblasts. To determine whether these lipids activated the same or different receptors, heterologous desensitization patterns were established among the three PLGFs by monitoring changes in intracellular Ca2+ in NIH3T3 fibroblasts. LPA cross-desensitized both the alkenyl-GP and cyclic-PA responses. Alkenyl-GP cross-desensitized the cyclic-PA response, but only partially desensitized the LPA response. Cyclic-PA only partially desensitized both the alkenyl-GP and LPA responses. We propose that pharmacologically distinct subsets of PLGF receptors exist that distinguish between cyclic-PA and alkenyl-GP, but are all activated by LPA. We provide evidence that the PSP24 receptor is selective for LPA and not activated by the other two PLGFs. RT-PCR and Northern blot analysis indicate the co-expression of mRNAs encoding the EDG-2, EDG-4, and PSP24 receptors in a variety of cell lines and tissues. However, the lack of mRNA expression for these three receptors in the LPA-responsive Rat-1 and Sp2-O-Ag14 cells suggests that a number of PLGF receptor subtypes remain unidentified.

L12 ANSWER 17 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:358695 BIOSIS
DOCUMENT NUMBER: PREV200300358695
TITLE: Fatty alcohol phosphates are subtype-selective agonists and antagonists of lysophosphatidic acid receptors.
AUTHOR(S): Virag, Tamas [Reprint Author]; Elrod, Don B.; Liliom, Karoly; Sardar, Vineet M.; Parrill, Abby L.; Yokoyama, Kazuaki; Durgam, Gangadhar; Miller, Duane D.; Tigyi, Gabor J.
CORPORATE SOURCE: Physiology, Univ. of Tennessee, 894 Union Ave., Memphis, TN, 38163, USA
tvirag@physiol.utmem.edu; don.elrod@lynntech.com; liliom@enzim.hu; vmsardar@yahoo.com; aparrill@memphis.edu; yokoyama@physiol.utmem.edu; gdurgam@utmem.edu; dmiller@utmem.edu; gtigyi@physiol.utmem.edu
SOURCE: FASEB Journal, (March 2003) Vol. 17, No. 4-5, pp. Abstract No. 123.8. http://www.fasebj.org/. e-file. Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. San Diego, CA, USA. April 11-15, 2003. FASEB.
ISSN: 0892-6638 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003
Last Updated on STN: 6 Aug 2003

AB Lysophosphatidic acid (LPA) activates the GPCRs LPA1, LPA2, and LPA3. A better understanding of the physiological and pathological role of LPA requires receptor subtype-specific ligands. Here, we report the synthesis and pharmacological characterization of fatty alcohol phosphates (FAPs) with saturated hydrocarbon chains, ranging from 4 to 22 carbon atoms. Selection of FAP as the lead structure was based on computational modeling as a predicted minimal structure that satisfies the two point pharmacophore model developed earlier. The 10 and 12 carbon chain FAPs (FAP 10 and FAP 12) were found to be specific agonists for LPA2, whilst selective antagonists for LPA3. FAP-12 was a weak antagonist for LPA1. Neither LPA1 nor LPA3 were activated by FAPs , whereas LPA2 was activated by C10-to-14 FAPs. Computational docking FAP 10 and 12 positioned these ligands in the LPA binding pocket in the LPA2 model. The inhibitory effect of FAP showed a strong dependence on the hydrocarbon chain length with C12 being the best in Xenopus oocytes and in LPA3-expressing RH7777 cells. FAP-12 did not activate or interfere with many GPCRs. These data suggest that FAPs are ligands of LPA receptors and that FAP 10 and FAP 12 are the first receptor subtype-specific agonists for LPA2.

L12 ANSWER 21 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:308725 BIOSIS
DOCUMENT NUMBER: PREV200200308725
TITLE: LPA analogs as agonists of the Edg2 LPA receptor.
AUTHOR(S): Erickson, James R. [Inventor, Reprint author]
CORPORATE SOURCE: El Cerrito, CA, USA
ASSIGNEE: Atairgin Technologies, Inc.
PATENT INFORMATION: US 6380177 20020430
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 30, 2002) Vol. 1257, No. 5. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 22 May 2002
Last Updated on STN: 22 May 2002

AB Applicant has probed the Edg2 lysophosphatidic acid (LPA) receptor with a series of LPA analogs to determine receptor activation. The present invention is drawn to a series of LPA analogs which function as Edg2 receptor agonists, and methods of using such compounds to activate the Edg2 receptor of the surface of a cell. The compounds of the invention comprise a glycerol backbone with an Sn1 ester-linked saturated or unsaturated alkyl group, substitutions of the hydroxyl group (--OH) at carbon two of the glycerol backbone, and optional replacement of the phosphate di-anion with either a hydroxyl group or a dimethylated phosphate. These LPA analogs may find uses in cancer and neurological disorders.

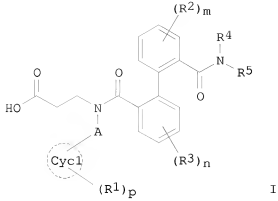
L12 ANSWER 22 OF 37 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:93755 BIOSIS
DOCUMENT NUMBER: PREV200200093755
TITLE: Agonist-induced internalization of lysophosphatidic acid-coupled Edg2 receptors via clathrin-dependent endocytosis.
AUTHOR(S): Murph, Mandi Michelle [Reprint author]; Scaccia, Launa [Reprint author]; Radhakrishna, Harish [Reprint author]

CORPORATE SOURCE: Biology, Georgia Institute of Technology, 315 First Drive, IBB No. 2228, Atlanta, GA, 30332, USA
SOURCE: Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. Supplement, pp. 89a. print.
Meeting Info.: 41st Annual Meeting of the American Society for Cell Biology. Washington DC, USA. December 08-12, 2001. American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jan 2002
Last Updated on STN: 25 Feb 2002

L12 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:950976 CAPLUS
DOCUMENT NUMBER: 140:16961
TITLE: Preparation of N-(2'-carbamoyl-1,1'-biphenyl-2-ylcarbonyl)-β-alanine derivatives as lysophosphatidic acid receptor antagonists
INVENTOR(S): Habashita, Hiromu; Terakado, Masahiko; Nakade, Shinji; Seko, Takuya
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 434 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099765	A1	20031204	WO 2003-JP6678	20030528 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003241833	A1	20031212	AU 2003-241833	20030528
EP 1533294	A1	20050525	EP 2003-733129	20030528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005256160	A1	20051117	US 2004-515653	20041124
PRIORITY APPLN. INFO.:			JP 2002-153592 A	20020528
			WO 2003-JP6678 W	20030528

OTHER SOURCE(S): MARPAT 140:16961
GI



I

AB The title compds. [I; A = C1-6 alkylene, C2-6 alkenylene, or C2-6 alkynylene each optionally substituted by 1-3 C1-4 alkyl group(s); the ring Cycl = C3-15 carbocyclic or 3- to 13-membered heterocyclic ring containing 1-4 N, 1-2 O, and/or 1-2 S atom(s); R1 = C1-4 alkyl, halo, cyano, trihalomethyl, OR6, SR7, NR8R9, NO2, CO2R10, CONR11R12, NR13COR14, SO2NR15R16, NR17SO2R18, S(O)R19, SO2R20; R6-R20 = H, C1-4 alkyl; R2, R3 = C1-4 alkyl, C1-4 alkoxy, halo; R4, R5 = H, C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl, R21O-C1-4 alkyl, R22R23N-C1-4 alkyl, etc.; or NR4R5 is combined together to represent 3- to 15-membered mono-, di-, or tricyclic heterocyclyl containing at least one N atom and optionally substituted by OR25; wherein R21, R22, R23, R25 = H, C1-4 alkyl, C2-6 acyl, trihaloacetyl; wherein m, n = an integer of 0-4; p = an integer of 0-5; when p, m, or n is ≥2, R1, R2, or R3 is same or different] or prodrugs or salts thereof are prepared These compds. engage in lysophosphatidic acid (LPA) receptor bonding, in particular EDG-2 and antagonism and hence are useful in the prevention and/or treatment of urol. diseases (symptoms associated with prostate-gland enlargement or neuropathic bladder, bone tumors of the spine, disk herniation, spinal canal stenosis, symptoms attributed to diabetes, lower urinary tract infections (e.g., obstruction of lower urinary tract), inflammation of lower urinary tract and polyuria), cancer-associated diseases (solid tumor, solid tumor metastasis, angiofibroma, myeloma, multiple myeloma, Kaposi's sarcoma, leukemia and wet metastasis of cancer), proliferative diseases (diseases accompanied by abnormal angiogenesis, blocked artery and lung fibrosis), inflammation/immune diseases (psoriasis, nephropathy, hepatitis and pneumonia), diseases caused by secretion disorder (Sjogren's syndrome) or brain-associated diseases (brain block, cerebral hemorrhage and cerebral or peripheral nerve disorder). Thus, 3-[N-[2-(2-carboxyphenyl)phenyl]-N-[2-(2,5-dimethoxyphenyl)ethyl]amino]propanoic acid-bound to Wang resin (preparation given) was condensed with 4-chlorobenzylamine using 1-hydroxybenzotriazole monohydrate and N,N-diisopropylcarbodiimide in DMF at room temperature for 16 h,

followed by treatment with a 9:1 mixture of CF3CO2H and H2O at room temperature for 1 h to give 3-[N-[2-[2-[(4-chlorobenzylamine)carbonyl]phenyl]carbonyl]-N-[2-(2,5-dimethoxyphenyl)ethyl]amino]propanoic acid (II). In an EDG-2 antagonism assay, II showed IC50 of 0.41 μmol/L for inhibiting the increase in cellular calcium ion-concentration in CHO cells over-expressing human EDG-2 gene. A tablet and an ampule containing II were prepared

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 2003:532340 CAPLUS
DOCUMENT NUMBER: 139:95489
TITLE: Lysophosphatidic acid (LPA) receptor agonists and antagonists, their preparation, and methods of use
INVENTOR(S): Miller, Duane D.; Tigyi, Gabor; Dalton, James T.; Sardar, Vineet M.; Elrod, Don B.; Xu, Huiping; Baker, Daniel L.; Wang, Dean; Liliom, Karoly; Fischer, David J.; Virag, Tamas; Nusser, Nora
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 73 pp., Cont.-in-part of U.S. Ser. No. 811,838.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003130237	A1	20030710	US 2001-953686	20010917 <--
US 2003027800	A1	20030206	US 2001-811838	20010319 <--
US 6875757	B2	20050405		
CA 2460319	A1	20030327	CA 2002-2460319	20020917 <--
WO 2003024402	A2	20030327	WO 2002-US29593	20020917 <--
WO 2003024402	A3	20040219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
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AU 2002336595	A1	20030401	AU 2002-336595	20020917 <--
EP 1427424	A2	20040616	EP 2002-773455	20020917
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JP 2005508319	T	20050331	JP 2003-528500	20020917
US 2005261252	A1	20051124	US 2005-67884	20050228
PRIORITY APPLN. INFO.:			US 2000-190370P	P 20000317
			US 2001-811838	A2 20010319
			US 2001-953686	A 20010917
			WO 2002-US29593	W 20020917

OTHER SOURCE(S): MARPAT 139:95489

AB The invention discloses LPA receptor ligand compds. X1C(Q1)CH(X3)C(Q2)X2 [≥1 X1-X3 = (HO)2POZ1 or (HO)2POZ2P(OH)OZ1, X1 and X2 linked together as OPO(OH)O, or X1 and X3 linked together as OPO(OH)NH; ≥1 X1-X3 = R1Y1A with each being the same or different when two of X1-X3 are R1Y1A, or X2 and X3 linked together as N(H)C(O)N(R1); optionally, one of X1-X3 = H; A = direct link, (CH2)k (k = 0-30), O; Y1 = (CH2)l (l = 1-30), O, C(O), S, NR2; Z1 = (CH2)m, O(CH2)m (m = 1- 50), C(R3)H, NH, O, S; Z2 = (CH2)N or (CH2)n (n = 1-50), O; Q1, Q2 = H2, :NR4, :O, combination of H and NR5R6; R1 (for each of X1-X3) = H, (un)branched C1-30 alkyl, (un)branched C2-30 alkenyl, (un)substituted (hetero)aromatic ring, etc.; R2-R8 = H, (un)branched C1-30 alkyl, (un)branched C2-30 alkenyl, etc.], as well as pharmaceutical compns. which include those compds. Also disclosed are methods of using such compds., which have activity as agonists or as antagonists of LPA receptors, the methods including inhibiting LPA activity on an LPA receptor, modulating LPA receptor activity, treating

cancer, enhancing cell proliferation, treating a wound, treating apoptosis or preserving or restoring function in a cell, tissue, or organ, culturing cells, preserving organ or tissue function, and treating a dermatol. condition.

L12 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:242130 CAPLUS
DOCUMENT NUMBER: 138:265691
TITLE: Lysophosphatidic acid (LPA) receptor agonists and antagonists, their preparation, and methods of use
INVENTOR(S): Miller, Duane D.; Tigyi, Gabor; Dalton, James T.; Sardar, Vineet M.; Elrod, Don B.; Xu, Huiping; Baker, Daniel L.; Wang, Dean; Liliom, Karoly; Fischer, David J.; Virag, Tamas; Nusser, Nora
PATENT ASSIGNEE(S): The University of Tennessee Research Corporation, USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024402	A2	20030327	WO 2002-US29593	20020917 <--
WO 2003024402	A3	20040219		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003130237	A1	20030710	US 2001-953686	20010917 <--
CA 2460319	A1	20030327	CA 2002-2460319	20020917 <--
AU 2002336595	A1	20030401	AU 2002-336595	20020917 <--
EP 1427424	A2	20040616	EP 2002-773455	20020917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005508319	T	20050331	JP 2003-528500	20020917
PRIORITY APPLN. INFO.:			US 2001-953686 A	20010917
			US 2000-190370P P	20000317
			US 2001-811838 A2	20010319
			WO 2002-US29593 W	20020917

OTHER SOURCE(S): MARPAT 138:265691
AB The invention discloses LPA receptor agonists and antagonists, as well as pharmaceutical compns. which include those compds. Compound preparation is described. Also disclosed are methods of using the compds., such methods including inhibiting LPA activity on an LPA receptor, modulating LPA receptor activity, treating cancer, enhancing cell proliferation, treating a wound, treating apoptosis or preserving or restoring function in a cell, tissue, or organ, culturing cells, preserving organ or tissue function, and treating a dermatol. condition.

L12 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:184214 CAPLUS
TITLE: Synthesis and biological evaluation of lysophosphatidic acid

antagonists

AUTHOR(S): Heasley, Brian H.; Macdonald, Timothy L.; Lynch, Kevin R.

CORPORATE SOURCE: Department of Chemistry, University of Virginia, Charlottesville, VA, 22904-4319, USA

SOURCE: Abstracts of Papers, 225th ACS National Meeting, New Orleans, LA, United States, March 23-27, 2003 (2003), MEDI-248. American Chemical Society: Washington, D. C.
CODEN: 69DSA4

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Lysophosphatidic acid (LPA) antagonists have potential applications as inhibitors of inflammation, cancer invasiveness, and atherogenesis. However, the detailed physiol. implications of LPA occupancy of individual receptors are largely unknown because subtype-selective agonists/antagonists are unavailable currently. Compds. containing bulky hydrophobic substituents at the 2-position of an N-acyl ethanolamide phosphate core structure have been shown to possess dual LPA1/LPA3 competitive antagonism. The most potent analog of this series (VPC12249) has been modified so as to optimize potency and selectivity at LPA receptors. Compds. containing variation in the acyl chain, linker region, and polar head group have been synthesized and screened for biol. activity at LPA receptors. Several dual antagonists of comparable activity have been discovered. One compound (VPC32104) shows improved potency and selectivity for LPA1. This paper will describe the sythetic methods and biol. evaluation of LPA receptor antagonists.

L12 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:276112 CAPLUS

DOCUMENT NUMBER: 136:289091

TITLE: Novel lysophosphatidic acid receptor agonists and antagonists

INVENTOR(S): Lynch, Kevin R.; MacDonald, Timothy L.; Heise, Christopher E.; Santos, Webster L.; Okusa, Mark D.

PATENT ASSIGNEE(S): University of Virginia Patent Foundation, USA

SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002029001	A2	20020411	WO 2001-US30936	20011003 <--
WO 2002029001	A3	20030821		
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AU 200196536	A	20020415	AU 2001-96536	20011003 <--
EP 1361872	A2	20031119	EP 2001-977415	20011003 <--
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US 2004122236	A1	20040624	US 2003-398305	20031015

US 7169818 B2 20070130
PRIORITY APPLN. INFO.: US 2000-237436P P 20001003
US 2001-264046P P 20010125
US 2001-297507P P 20010613
WO 2001-US30936 W 20011003
OTHER SOURCE(S): MARPAT 136:289091
AB The present invention is directed to compns. comprising lysophosphatidic acid analogs and methods of using such analogs as agonist or antagonists of lysophosphatidic acid (LPA) receptor activity. In addition the invention is directed to LPA receptor agonists that vary in the degree of selectivity at individual LPA receptors (i.e. LPA1, LPA2 and LPA3). More particularly the present invention is directed to LPA analogs wherein the glycerol is replaced with ethanolamine and a variety of substitutions have been linked at the second carbon atom.

L12 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:713600 CAPLUS
DOCUMENT NUMBER: 135:267219
TITLE: Synthesis of lysophosphatidic acid receptor agonists and antagonists and their use for cancer inhibition, wound healing, and enhancement of cell proliferation
INVENTOR(S): Miller, Duane D.; Tigyi, Gabor; Dalton, James T.; Sardar, Vineet M.; Elrod, Don B.; Xu, Huiping; Baker, Daniel L.; Wang, Dean; Liliom, Karoly; Fischer, David J.; Virag, Tamas; Nusser, Nora
PATENT ASSIGNEE(S): University of Tennessee Research Corporation, USA
SOURCE: PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001071022	A2	20010927	WO 2001-US8729	20010319 <--
WO 2001071022	A3	20020404		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2402038	A1	20010927	CA 2001-2402038	20010319 <--
AU 200149263	A	20011003	AU 2001-49263	20010319 <--
EP 1263752	A2	20021211	EP 2001-922465	20010319 <--
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JP 2004506604	T	20040304	JP 2001-569403	20010319

PRIORITY APPLN. INFO.: US 2000-190370P P 20000317
WO 2001-US8729 W 20010319
OTHER SOURCE(S): MARPAT 135:267219
AB The present invention relates to lysophosphatidic acid (LPA) analogs and cyclic derivs. of the analogs as well as pharmaceutical compns. which include those compds. Also disclosed are methods of using such compds., which have activity as agonists or as antagonists of LPA receptors; such methods including inhibiting LPA

activity on an LPA receptor, modulating LPA receptor activity, treating cancer, enhancing cell proliferation, and treating a wound. Thus, 2-amino-3-oxo-3-(tetradecylamino)propyl dihydrogen phosphate (I), 2-(acetylamino)-3-oxo-3-(tetradecylamino)propyl dihydrogen phosphate (II), and 1,2-(3-octadecyloxypropane)-bis(dihydrogen phosphate) (III) were synthesized. The cytotoxicity of these compds. on prostate cancer cell lines was determined The IC50's observed were 0.7 ± 0.1 for I on PC-3 cells, 0.7 ± 0.1 for II on DU145 cells, and 3.1 ± 3.2 for III on LNCaP cells. Addnl., phosphoric acid monododecyl ester (IV) was prepared and screened in Xenopus oocytes (which produce the PSP24 receptor) and in recombinant RH7777 cells producing Edg-2, Edg-4, and Edg-7 receptors. In Xenopus IV inhibited LPA-induced chloride currents with an IC50 value of about 8.1 nM. In Edg-2 and Edg-4-expressing RH7777 cells IV significantly inhibited the Ca2+ responses while in Edg-7-expressing cells this compound increased the Ca2+ responses.

L12 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:688874 CAPLUS
DOCUMENT NUMBER: 135:341872
TITLE: Assessment of agonism at G-protein coupled receptors by phosphatidic acid and lysophosphatidic acid in human embryonic kidney 293 cells
AUTHOR(S): Alderton, Forbes; Sambi, Balwinder; Tate, Rothwelle; Pyne, Nigel J.; Pyne, Susan
CORPORATE SOURCE: Department of Physiology and Pharmacology, Strathclyde Institute for Biomedical Sciences, University of Strathclyde, Glasgow, G4 0NR, UK
SOURCE: British Journal of Pharmacology (2001), 134(1), 6-9
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several different mol. species of phosphatidic acid (PA) bind to a G-protein coupled receptor (GPCR) to induce activation of the p42/p44 mitogen-activated protein kinase (p42/p44 MAPK) pathway in HEK 293 cells. PA is active at low nanomolar concns. and the response is sensitive to pertussis toxin (which uncouples GPCRs from Gi/o). The de-acylated product of PA, lysophosphatidic acid (LPA), which binds to members of the endothelial differentiation gene (EDG) family of receptors also stimulated p42/p44 MAPK in a pertussis toxin sensitive manner, but with an .apprx. 100-1000 fold lower potency compared with the different mol. species of PA. RT-PCR using gene-specific primers showed that HEK 293 cells express EDG2 and PSP24, the latter being a lipid binding GPCR out with the EDG cluster. We conclude that PA is a novel high potency GPCR agonist.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'STNGUIDE' ENTERED AT 12:59:51 ON 03 JUL 2007
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L1       108930 S NEPHROPATHY
L2        10068 S LYSOPHOSPHATIDIC ACID
L3          419 S EDG RECEPTOR
L4            0 S L1 AND L2 AND L3
L5          190 S L2 AND L3
L6           87 DUP REM L5 (103 DUPLICATES REMOVED)
L7            4 S L6 AND THERAPY
L8            4 S L6 AND MODULATOR
L9         1072 S L2 (S)(AGONIST OR ANALOG OR ANTAGONIST OR INHIBITOR)
L10         695 S L9 AND PD<=20031211
L11         303 DUP REM L10 (392 DUPLICATES REMOVED)
L12          37 S L11 (S)(EDG-2 OR EDG2 OR LPA1)

     FILE 'STNGUIDE' ENTERED AT 11:23:39 ON 03 JUL 2007

     FILE 'MEDLINE, BIOSIS, CAPLUS' ENTERED AT 11:25:48 ON 03 JUL 2007

     FILE 'STNGUIDE' ENTERED AT 11:25:50 ON 03 JUL 2007

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                 (EDG(W)RECEPTOR)
             0 ENDOGENOUS
             2 EXPRESSION
L13          0 L3(S)(ENDOGENOUS(W)EXPRESSION)

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             0 RECEPTOR
             0 EDG RECEPTOR
                 (EDG(W)RECEPTOR)
             0 ENDOGENOUS
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L14          0 L3 AND (ENDOGENOUS(W)EXPRESSION)

=> S L3 AND Expression
             0 EDG
             0 RECEPTOR
             0 EDG RECEPTOR
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                (EDG(W)RECEPTOR)
             2 EXPRESSION
L15          0 L3 AND EXPRESSION

=> S L3 AND Cell
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             0 RECEPTOR
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                (EDG(W)RECEPTOR)
            15 CELL
L16          0 L3 AND CELL

=> S L2(W)receptor
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             6 ACID
             1 ACIDS
             6 ACID
                (ACID OR ACIDS)
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FULL ESTIMATED COST                                     0.48     103.51

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FILE 'BIOSIS' ENTERED AT 13:04:48 ON 03 JUL 2007
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L20        196 L3 AND EXPRESSION

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nested terms that are not separated by a logical operator.

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FIELD CODE - 'AND' OPERATOR ASSUMED 'L83(S)KIDNEY'
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L21  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2007 ACS on STN
AB   Lysophosphatidic acid (LPA), a major member of the bioactive
     lysophospholipids in serum, possesses diverse physiol. activities
     including cell proliferation.  Recently, three endothelial differentiation
     gene (EDG) family receptors, including EDG-2 (LPA1), EDG-4 (LPA2), and
     EDG-7 (LPA3), have been identified as LPA receptors.  The role of LPA and
     their receptors in mesangial cell physiol. is not clearly understood.
     This study examined the expression profile of EDG
     receptors as a function of cell d. and the participation of
     EDG receptors in human mesangial cell proliferation by
     LPA.  We showed that mesangial cells express all three EDG family LPA
     receptors in a cell d.-dependent manner.  EDG-7 maximally expressed at
     sparse cell d. and minimally expressed in dense cell population.  The
     EDG-2 expression pattern was opposite to the EDG-7.  No changes
     in EDG-4 expression as a function of cell d. were noted.  DNA
     synthetic rate was greater in sparse cell d. compared with dense cell
     population and followed a similar pattern with EDG-7 expression.
     Comparative studies in sparse and dense cell d. indicated that EDG-7 was
     pos. associated, whereas EDG-2 was neg. associated with cell proliferation
rate.
     LPA induced mesangial cell proliferation by 1.5- to 3.5-fold.
     Dioctanoylglycerol pyrophosphate, an antagonist for EDG-7, almost
     completely inhibited mesangial cell proliferation induced by LPA.  We
     suggest that EDG-7 regulates LPA-mediated mesangial cell proliferation.
     Addnl., these data suggest that EDG-7 and EDG-2 LPA receptors play a
     diverse role as proliferative and antiproliferative, resp., in mesangial
     cells.  Regulation of EDG family receptors may be importantly linked to
     mesangial cell-proliferative processes.

L21  ANSWER 2 OF 3  CAPLUS  COPYRIGHT 2007 ACS on STN
AB   RGS proteins finely tune heterotrimeric G-protein signaling.  Implying the
     need for such fine-tuning in the developing vascular system, in situ
     hybridization revealed a striking and extensive expression
     pattern of Rgs5 in the arterial walls of E12.5-E17.5 mouse embryos.  The
     distribution and location of the Rgs5-pos. cells typified that of
     pericytes and strikingly overlapped the known expression pattern
     of platelet-derived growth factor receptor (PDGFR)-β.  Both E14.5
     PDGFR-β- and platelet-derived growth factor (PDGF)-B-deficient mice
     exhibited markedly reduced levels of Rgs5 in their vascular plexa and
     small arteries.  This likely reflects the loss of pericytes in the mutant
     mice.  RGS5 acts as a potent GTPase activating protein for Giα and
     Gqα and it attenuated angiotensin II-, endothelin-1-,
     sphingosine-1-phosphate-, and PDGF-induced ERK-2 phosphorylation.
     Together these results indicate that RGS5 exerts control over PDGFR-β
     and GPCR-mediated signaling pathways active during fetal vascular
     maturation.

L21  ANSWER 3 OF 3  EMBASE  COPYRIGHT (c) 2007 Elsevier B.V. All rights
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AB   Recently, a family of G-protein-coupled receptors named endothelial
     differentiation gene (Edg) receptor family has been
     identified, which are specifically activated by the two serum lipids,
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sphingosine-1-phosphate and lysophosphatidic acid. Sphingosine-1-phosphate can also act intracellularly to release Ca(2+) from intracellular stores. Since in several cell types, G-protein-coupled lysophosphatidic acid or sphingosine-1-phosphate receptors mobilize Ca(2+) in the absence of a measurable phospholipase C stimulation, it was analysed here whether intracellular sphingosine-1-phosphate production was the signalling mechanism used by extracellular sphingosine-1-phosphate for mobilization of stored Ca(2+). Sphingosine-1-phosphate and the low affinity sphingosine-1-phosphate receptor agonist, sphingosylphosphorylcholine, induced a rapid, transient and nearly complete pertussis toxin-sensitive Ca(2+) mobilization in human embryonic kidney (HEK-293) cells. The G-protein-coupled sphingosine-1-phosphate receptors, Edg-1, Edg-3 and Edg-5, were found to be endogenously expressed in these cells. Most interestingly, sphingosine-1-phosphate and sphingosylphosphorylcholine did not induce a measurable production of inositol-1,4,5-trisphosphate or accumulation of inositol phosphates. Instead, sphingosine-1-phosphate and sphingosylphosphorylcholine induced a rapid and transient increase in production of intracellular sphingosine-1-phosphate with a maximum of about 1.4-fold at 30 s. Stimulation of sphingosine-1-phosphate formation by sphingosine-1-phosphate and sphingosylphosphorylcholine was fully blocked by pertussis toxin, indicating that extracellular sphingosine-1-phosphate via endogenously expressed G(i)-coupled receptors induces a stimulation of intracellular sphingosine-1-phosphate production. As sphingosine-1-phosphate- and sphingosylphosphorylcholine-induced increases in intracellular Ca(2+) were blunted by sphingosine kinase inhibitors, this sphingosine-1-phosphate production appears to mediate Ca(2+) signalling by extracellular sphingosine-1-phosphate and sphingosylphosphorylcholine in HEK-293 cells. .COPYRGT. 2001 Elsevier Science B.V.

=> D ibib l21 1-3

L21 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1075963 CAPLUS
DOCUMENT NUMBER: 142:20821
TITLE: Cell density-dependent expression of EDG family receptors and mesangial cell proliferation: Role in lysophosphatidic acid-mediated cell growth
AUTHOR(S): Xing, Yiding; Ganji, Shobha H.; Noh, Jung W.; Kamanna, Vaijinath S.
CORPORATE SOURCE: Medical Research Service, Department of Veterans Affairs Healthcare System, Long Beach, 90822, USA
SOURCE: American Journal of Physiology (2004), 287(6, Pt. 2), F1250-F1257
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:212940 CAPLUS
DOCUMENT NUMBER: 139:1403
TITLE: Pericyte-specific expression of RGS5: implications for PDGF and EDG receptor signaling during vascular maturation
AUTHOR(S): Cho, Hyeseon; Kozasa, Tohru; Bondjers, Cecilia; Betsholtz, Christer; Kehrl, John H.
CORPORATE SOURCE: National Institute of Allergy and Infectious Diseases,

	Lab. of Immunoregulation, National Institute of Allergy and Infectious Diseases, Bethesda, MD, 20892-1876, USA
SOURCE:	FASEB Journal (2003), 17(3), 440-442, 10.1096/fj.02-0340fje CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER:	Federation of American Societies for Experimental Biology
DOCUMENT TYPE:	Journal
LANGUAGE:	English
REFERENCE COUNT:	27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 3 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER:	2001084181 EMBASE
TITLE:	Stimulation of intracellular sphingosine-1-phosphate production by G-protein-coupled sphingosine-1-phosphate receptors.
AUTHOR:	Meyer zu Heringdorf D.; Lass H.; Kuchar I.; Lipinski M.; Alemany R.; Rumenapp U.; Jakobs K.H.
CORPORATE SOURCE:	D. Meyer zu Heringdorf, Institut fur Pharmakologie, Universitatsklinikum Essen, Hufelandstrasse 55, D-45122 Essen, Germany. meyer-heringdorf@uni-essen.de
SOURCE:	European Journal of Pharmacology, (2 Mar 2001) Vol. 414, No. 2-3, pp. 145-154. . Refs: 36 ISSN: 0014-2999 CODEN: EJPHAZ
PUBLISHER IDENT.:	S 0014-2999(01)00789-0
COUNTRY:	Netherlands
DOCUMENT TYPE:	Journal; Article
FILE SEGMENT:	030 Pharmacology 037 Drug Literature Index
LANGUAGE:	English
SUMMARY LANGUAGE:	English
ENTRY DATE:	Entered STN: 6 Apr 2001 Last Updated on STN: 6 Apr 2001

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NEWS 29	SEP 26	WPIDS, WPINDEX, and WPIX coverage of Chinese and and Korean patents enhanced
NEWS 30	SEP 29	IFICLS enhanced with new super search field
NEWS 31	SEP 29	EMBASE and EMBAL enhanced with new search and

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                  display fields
 NEWS 32  SEP 30  CAS patent coverage enhanced to include exemplified
                  prophetic substances identified in new Japanese-
                  language patents

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=> S ((lysophophatidic acid OR LPA) OR (EDG receptor)) (S) Mesangial AND
pd<=20031211
   1 FILES SEARCHED...
L1          55 ((LYSOPHOPHATIDIC ACID OR LPA) OR (EDG RECEPTOR)) (S) MESANGIAL
               AND PD<=20031211

=> Dup Rem L1
PROCESSING COMPLETED FOR L1
L2           21 DUP REM L1 (34 DUPLICATES REMOVED)
                ANSWERS '1-15' FROM FILE MEDLINE
                ANSWERS '16-19' FROM FILE BIOSIS
                ANSWER '20' FROM FILE CAPLUS
                ANSWER '21' FROM FILE EMBASE

=> D Ibib Abs L2 1-15

L2   ANSWER 1 OF 21     MEDLINE on STN                  DUPLICATE 1
ACCESSION NUMBER:   2002464486     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 12224049
```

TITLE: LPA as a determinant of mesangial growth and apoptosis.
AUTHOR: Inoue Chiyoko N
CORPORATE SOURCE: Department of Pediatrics, Japanese Red Cross Sendai Hospital, Sendai, Japan.. cnagano@sendai.jrc.or.jp
SOURCE: Seminars in nephrology, (2002 Sep) Vol. 22, No. 5, pp. 415-22. Ref: 38
Journal code: 8110298. ISSN: 0270-9295.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200211
ENTRY DATE: Entered STN: 12 Sep 2002
Last Updated on STN: 13 Dec 2002
Entered Medline: 22 Nov 2002

AB Mesangial cell proliferation is a prominent feature of progression in many forms of renal diseases, including immunoglobulin A nephropathy, lupus nephritis, hemolytic uremic syndrome, and diabetic nephropathy. Platelet-derived growth factor (PDGF) has received much attention as the major mediator of mesangial cell proliferation by autocrine/paracrine mechanisms involving up-regulation of mesangial PDGF and its receptor on mesangial cells. In this review, we wish to spotlight lysophosphatidic acid (LPA), which in combination with PDGF, undoubtedly plays a key role as an autocrine and paracrine mediator in regulating mesangial cell growth. We not only showed that PDGF acts as a bimodal molecule for mesangial cells, inducing mesangial cell proliferation and death simultaneously, but also showed that LPA is a survival factor suppressing PDGF-induced mesangial cell death, thereby remarkably enhancing mesangial mitogenic response by PDGF. We believe that a better understanding of the mechanisms of mesangial cell proliferation by the combined action of PDGF and LPA could lead to novel diagnostic as well as therapeutic strategies, and thus help to better control proliferative glomerulonephritis.

L2 ANSWER 2 OF 21 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002390033 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12110510
TITLE: LPA is a novel lipid regulator of mesangial cell hexokinase activity and HKII isoform expression.
AUTHOR: Coy Platina E; Taneja Navin; Lee Iris; Hecquet Claudie; Bryson Jane M; Robey R Brooks
CORPORATE SOURCE: Section of Nephrology, Department of Medicine, University of Illinois at Chicago College of Medicine, Chicago, Illinois 60612-7315, USA.
SOURCE: American journal of physiology. Renal physiology, (2002 Aug) Vol. 283, No. 2, pp. F271-9.
Journal code: 100901990. ISSN: 0363-6127.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 26 Jul 2002
Last Updated on STN: 18 Dec 2002

Entered Medline: 8 Aug 2002

AB The prototypical extracellular phospholipid mediator, lysophosphatidic acid (LPA), exhibits growth factor-like properties and represents an important survival factor in serum. This potent mesangial cell mitogen is increased in conditions associated with glomerular injury. It is also a known activator of the classic mitogen-activated protein kinase (MAPK) pathway, which plays an important role in the regulation of mesangial cell hexokinase (HK) activity. To better understand the mechanisms coupling metabolism to injury, we examined the ability of LPA to regulate HK activity and expression in cultured murine mesangial cells. LPA increased total HK activity in a concentration- and time-dependent manner, with maximal increases of >50% observed within 12 h of exposure to LPA concentrations > or =25 microM (apparent ED(50) 2 microM). These effects were associated with increased extracellular signal-regulated kinase (ERK) activity and were prevented by the pharmacological inhibition of either MAPK/ERK kinase or protein kinase C (PKC). Increased HK activity was also associated with increased glucose (Glc) utilization and lactate accumulation, as well as selectively increased HKII isoform abundance. The ability of exogenous LPA to increase HK activity was both Ca2+ independent and pertussis toxin insensitive and was mimicked by LPA-generating phospholipase A2. We conclude that LPA constitutes a novel lipid regulator of mesangial cell HK activity and Glc metabolism. This regulation requires sequential activation of both Ca2+-independent PKC and the classic MAPK pathway and culminates in increased HKII abundance. These previously unrecognized metabolic consequences of LPA stimulation have both physiological and pathophysiological implications. They also suggest a novel mechanism whereby metabolism may be coupled to cellular injury via extracellular lipid mediators.

L2 ANSWER 3 OF 21 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER:	2002129834 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 11829737
TITLE:	Role of Rac and Cdc42 in lysophosphatidic acid-mediated cyclo-oxygenase-2 gene expression.
AUTHOR:	Hahn Angelika; Barth Holger; Kress Michaela; Mertens Peter R; Goppelt-Struebe Margarete
CORPORATE SOURCE:	Medizinische Klinik IV, Universitat Erlangen-Nurnberg, Loschgestr. 8, D-91054 Erlangen, Germany.
SOURCE:	The Biochemical journal, (2002 Feb 15) Vol. 362, No. Pt 1, pp. 33-40. Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY:	England: United Kingdom
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200203
ENTRY DATE:	Entered STN: 28 Feb 2002 Last Updated on STN: 24 Mar 2002 Entered Medline: 22 Mar 2002

AB The role of Rho proteins in lysophosphatidic acid (LPA)-mediated induction of cyclo-oxygenase-2 (Cox-2) was investigated in renal mesangial cells. Previous studies had shown that toxin B, an inhibitor of Rho, Rac and Cdc42, suppressed Cox-2 induction. A role for RhoA in pertussis toxin-sensitive LPA signalling was excluded with C3 transferase from Clostridium limosum, used as the fusion toxin C2IN-C3 (where C2IN is part of the C2I toxin of C. botulinum). Incubation of the cells with C2IN-C3 disrupted cytosolic actin stress fibres, but had no effect on Cox-2 induction. Similarly, activation of p42/44 mitogen-activated protein kinase (MAP kinase), an upstream step in Cox-2 induction, was inhibited by toxin B, but not affected by C2IN-C3. Upon

treatment with toxin B, focal adhesion kinase and paxillin were dephosphorylated at tyrosine residues and the actin cytoskeleton was completely destroyed. An intact cytoskeleton, however, was not required for p42/44 MAP-kinase activation or Cox-2 induction, as shown by the actin-depolymerizing agent cytochalasin D. Toxin B did not influence functionality of LPA receptors, because G(i)-mediated Ca(2+) release from intracellular stores remained unchanged. Within 1 h, toxin B inactivated and translocated RhoA and Cdc42 to the cellular membranes. Within the same time frame, monoglucosylated Rac1 was degraded. Direct stimulation of Rho proteins by cytotoxic necrotizing factor type 1 (CNF1) induced Cox-2 expression, which was sensitive to inhibition of the MAP-kinase pathway by PD98059, but not to an inhibitor of RhoA kinase. By exclusion of RhoA and non-specific cytoskeletal effects, the results in the present study indicate an important role for Rac and/or Cdc42 in pertussis toxin-sensitive LPA-mediated Cox-2 induction.

L2 ANSWER 4 OF 21 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001347253 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11410109
TITLE: Bimodal effects of platelet-derived growth factor on rat mesangial cell proliferation and death, and the role of lysophosphatidic acid in cell survival.
AUTHOR: Inoue C N; Nagano I; Ichinohasama R; Asato N; Kondo Y; Iinuma K
CORPORATE SOURCE: Department of Pediatrics, Tohoku University School of Medicine, Sendai, Japan.. cnagano@sendai.jrc.or.jp
SOURCE: Clinical science (London, England : 1979), (2001 Jul) Vol. 101, No. 1, pp. 11-9.
Journal code: 7905731. ISSN: 0143-5221.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 13 Aug 2001
Last Updated on STN: 13 Aug 2001
Entered Medline: 9 Aug 2001
AB Although mesangial cell death has been shown to be correlated with mesangial cell mitosis in vivo, little is known about how these two apparently opposite events are regulated. We show that the addition of platelet-derived growth factor (PDGF; 10-50 ng/ml) to primary cultured rat mesangial cells for 24 h caused continuous proliferation along with simultaneous cell death. This process was accompanied by the fragmentation of DNA into nucleosomal oligomers, the development of apoptotic morphological changes in the nucleus, and increased expression of p53. Accumulation of lactate dehydrogenase (LDH) was also observed in the culture medium, suggesting that both apoptosis and necrosis are involved in the cell death mechanisms observed. We also observed that addition of 30 microM lysophosphatidic acid (LPA) to the culture medium greatly suppressed PDGF-induced cell death, leading to synergistically enhanced mesangial cell proliferation. DNA fragmentation, p53 expression and LDH release were all suppressed by LPA. We suggest that PDGF is a bifunctional molecule in mesangial cells that evokes both cell proliferation and cell death simultaneously, whereas LPA is a survival factor. We speculate that PDGF and LPA may play important roles in the progression or exacerbation of proliferative glomerulonephritis.

L2 ANSWER 5 OF 21 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001078247 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10976101

TITLE: Induction of connective tissue growth factor by activation of heptahelical receptors. Modulation by Rho proteins and the actin cytoskeleton.
AUTHOR: Hahn A; Heusinger-Ribeiro J; Lanz T; Zenkel S; Goppelt-Struebe M
CORPORATE SOURCE: Medizinische Klinik IV, Universitat Erlangen-Nurnberg, Loschgestrasse 8, D-91054 Erlangen, Germany.
SOURCE: The Journal of biological chemistry, (2000 Dec 1) Vol. 275, No. 48, pp. 37429-35. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 11 Jan 2001

AB Expression of connective tissue growth factor (CTGF) was induced in renal mesangial cells by activation of heptahelical receptors by serotonin (5-HT) and lysophosphatidic acid (LPA). Induction of CTGF mRNA was transient with maximal expression after 1 to 2 h, whereas induction of CTGF by transforming growth factor beta (TGF-beta) increased over time. In contrast to the induction of other early response genes (Egr-1 and cyclooxygenase-2), LPA-mediated induction of CTGF was pertussis toxin-insensitive and independent of p42/44 MAP kinase activation. 5-HT-mediated CTGF induction was due to activation of 5-HT(2A) receptors and likewise independent of p42/44 MAP kinase activation. Upon stimulation, enhanced levels of CTGF protein were detected in cellular homogenates, whereas no protein was detectable in cell culture supernatants. Inhibition of proteins of the Rho family by toxin B abrogated basal as well as CTGF expression stimulated by LPA, 5-HT, and TGF-beta. Inhibition of the downstream mediator of RhoA, the Rho kinase by Y-27632 partially reduced induction of CTGF by LPA and TGF-beta. Toxin B not only affected gene expression, but disrupted the actin cytoskeleton similarly as observed after treatment with cytochalasin D. Disassembly of actin stress fibers by cytochalasin D partially reduced basal and stimulated CTGF expression. These data indicate that an intact actin cytoskeleton is critical for the expression of CTGF. Elimination of the input of Rho proteins by toxin B, however, was significantly more effective and their effect on CTGF expression thus goes beyond disruption of the cytoskeleton. These findings thus establish activation of heptahelical receptors coupled to pertussis toxin-insensitive G proteins as a novel signaling pathway to induce CTGF. Proteins of the Rho family and an intact cytoskeleton were identified as critical determinants of CTGF expression induced by LPA and 5-HT, and also by TGF-beta.

L2 ANSWER 6 OF 21 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2000429716 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10945862
TITLE: Synergistic stimulation of airway smooth muscle cell mitogenesis.
AUTHOR: Ediger T L; Toews M L
CORPORATE SOURCE: Department of Pharmacology, University of Nebraska Medical Center, Omaha68198-6260, USA.
SOURCE: The Journal of pharmacology and experimental therapeutics, (2000 Sep) Vol. 294, No. 3, pp. 1076-82. Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 22 Sep 2000
Last Updated on STN: 22 Sep 2000
Entered Medline: 12 Sep 2000

AB Previous studies showed that human airway smooth muscle (HASM) cells treated with lysophosphatidic acid (LPA), a pertussis toxin (PTX)-sensitive G protein-coupled (GPC) mitogen, simultaneously with epidermal growth factor (EGF), a receptor tyrosine kinase (RTK) mitogen, exhibit markedly synergistic stimulation of mitogenesis. We now show that the RTK mitogens basic fibroblast growth factor, insulin-like growth factor-1, insulin, platelet-derived growth factor-AA, and platelet-derived growth factor-BB, as well as transforming growth factor-beta, all induced synergistic stimulation of mitogenesis in the presence of LPA. The PTX-sensitive GPC mitogens carbachol and endothelin-1 and the PTX-insensitive GPC mitogens sphingosine-1-phosphate and thrombin exhibited synergistic stimulation together with EGF. Several RTK-RTK growth factor pairs and GPC-GPC mitogen pairs were also synergistic. HASM cells showed synergistic responses to serum plus EGF but not to serum plus LPA. Testing various other cell types showed that synergism between LPA and EGF occurred in other smooth muscle cells because both vascular smooth muscle cells and mesangial cells exhibited synergism. Additionally, human fetal lung fibroblasts also showed striking synergism. These results indicate that HASM cells can respond synergistically to a wide variety of mitogen combinations and that this synergism is a feature shared with other contractile cell types.

L2 ANSWER 7 OF 21 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000088653 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10620497
TITLE: The platelet-derived-growth-factor receptor, not the epidermal-growth-factor receptor, is used by lysophosphatidic acid to activate p42/44 mitogen-activated protein kinase and to induce prostaglandin G/H synthase-2 in mesangial cells.
AUTHOR: Goppelt-Struebe M; Fickel S; Reiser C O
CORPORATE SOURCE: Medizinische Klinik IV, Universitat Erlangen-Nurnberg, Loschgestrasse 8, D-91054 Erlangen, Germany.. Goppelt-Struebe@rzmail.uni-erlangen.de
SOURCE: The Biochemical journal, (2000 Jan 15) Vol. 345 Pt 2, pp. 217-24.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 14 Mar 2000
Last Updated on STN: 18 Dec 2002
Entered Medline: 2 Mar 2000

AB In renal mesangial cells, activation of protein tyrosine kinase receptors may increase the activity of mitogen-activated protein (MAP) kinases and subsequently induce expression of prostaglandin G/H synthase-2 (PGHS-2, cyclo-oxygenase-2). As examples, platelet-derived growth factor (PDGF) and epidermal growth factor (EGF) were shown to transiently enhance p42/44 MAP kinase activity, which was an essential step in the induction of PGHS-2 mRNA and protein. Inhibitors of receptor kinase activities, tyrphostins AG1296 and AG1478, specifically inhibited the effects of PDGF and EGF respectively. Activation of p42/44 and p38 MAP kinases and PGHS-2 induction were also mediated by lysophosphatidic acid (LPA), which binds

to pertussis-toxin-sensitive G-protein-coupled receptors. LPA stimulation was inhibited by AG1296, but not AG1478, indicating involvement of the PDGF receptor kinase in LPA-mediated signalling. This was confirmed by pertussis-toxin-sensitive tyrosine phosphorylation of the PDGF receptor by LPA, whereas no phosphorylation of the EGF receptor was detected. For comparison, 5-hydroxytryptamine ('serotonin')-mediated signalling was only partially inhibited by AG1296, and also not affected by AG1478. A strong basal AG1296-sensitive tyrosine phosphorylation of the PDGF receptor and a set of other proteins was observed, which by itself was not sufficient to induce p42/44 MAP kinase activation, but played an essential role not only in LPA- but also in phorbol ester-mediated activation. Taken together, the PDGF receptor, but not the EGF receptor, is involved in LPA -mediated MAP kinase activation and PGHS-2 induction in primary mesangial cells, where both protein kinase receptors are present and functionally active.

L2 ANSWER 8 OF 21 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1999189185 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10087253
TITLE: Lysophosphatidic acid and mesangial cells: implications for renal diseases.
AUTHOR: Inoue C N; Epstein M; Forster H G; Hotta O; Kondo Y; Iinuma K
CORPORATE SOURCE: Department of Pediatrics, Tohoku University School of Medicine, 1-1 Seiryo-machi, Sendai 980-8574, Japan.
SOURCE: Clinical science (London, England : 1979), (1999 Apr) Vol. 96, No. 4, pp. 431-6. Ref: 40
Journal code: 7905731. ISSN: 0143-5221.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 18 Jun 1999
Last Updated on STN: 18 Jun 1999
Entered Medline: 10 Jun 1999

AB The last decade has witnessed a phenomenal increase in our understanding of the biological role of lysophosphatidic acid (LPA) and has led to an appreciation of this critical serum-derived growth factor released from platelets. We herein summarize recent observations that collectively support the hypothesis that LPA may play a key role in the pathogenesis of initiation and progression of proliferative glomerulonephritis. LPA synergistically stimulates mesangial cell proliferation in combination with platelet-derived growth factor in primary culture. The mechanism of co-mitogenesis is likely to be mediated by the prolonged activation of mitogen-activated protein kinase which is stimulated by platelet-derived growth factor and LPA through different mechanisms. LPA contracts cultured mesangial cells and has properties in common with other pressor molecules including mobilization of intracellular Ca2+ and promotion of Ca2+ entry through dihydropyridine-sensitive calcium channels. LPA receptor mRNA has been identified in isolated glomeruli dissected from renal biopsy samples of patients with IgA nephropathy. All of these facts have led us to postulate that LPA is produced within glomeruli and that LPA's mitogenic as well as haemodynamic action contribute to the pathological process of mesangial proliferative glomerulonephritis. The possible production of LPA as an autocrine factor from mesangial cells themselves has also been discussed.

L2 ANSWER 9 OF 21 MEDLINE on STN DUPLICATE 9

ACCESSION NUMBER: 1998161785 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9494074
TITLE: Lysophosphatidic acid-mediated signal-transduction pathways involved in the induction of the early-response genes prostaglandin G/H synthase-2 and Egr-1: a critical role for the mitogen-activated protein kinase p38 and for Rho proteins.
AUTHOR: Reiser C O; Lanz T; Hofmann F; Hofer G; Rupprecht H D; Goppelt-Struebe M
CORPORATE SOURCE: Medizinische Klinik IV, Universitat Erlangen-Nurnberg, Loschgestr. 8, D-91054 Erlangen, Germany.
SOURCE: The Biochemical journal, (1998 Mar 15) Vol. 330 (Pt 3), pp. 1107-14.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 29 May 1998
Last Updated on STN: 18 Dec 2002
Entered Medline: 21 May 1998

AB During inflammatory processes of the kidney, lesions of the glomerulus lead to aggregation of thrombocytes and infiltration of macrophages, which can release bioactive mediators. One of these important signalling molecules is lysophosphatidic acid (LPA). Incubation of rat mesangial cells with LPA induced mRNA and protein expression of the early-response genes pghs-2 (for prostaglandin G/H synthase-2/cyclo-oxygenase-2) and egr-1. As shown by antisense experiments, induction of egr-1 was related to the strong mitogenic effect of LPA. LPA-mediated gene expression was inhibited by pertussis toxin, indicating coupling to G-proteins of the Gi family. Specific inhibition of proteins of the small G-protein subfamily Rho with toxin B from Clostridium difficile led to changes in mesangial cell morphology without induction of apoptosis. LPA-mediated expression of pghs-2 and egr-1 was reduced to base-line levels by toxin B, indicating a role for Rho proteins in LPA-mediated gene induction. Of the two mitogen-activated protein kinase (MAPK) pathways investigated, the MAPK kinase-extracellular signal-regulated kinase pathway was involved in the induction of both pghs-2 and egr-1 mRNA expression, as shown by the inhibitory effect of PD98059. Activation of the MAPK p38, however, was only related to pghs-2 expression, whereas egr-1 expression was not affected by treatment of mesangial cells with the specific inhibitor SB203580. Taken together our data provide evidence that LPA-mediated activation of MAPK kinase and Rho proteins leads to the induction of the functionally distinct early-response genes pghs-2 and egr-1, whereas activation of MAPK p38 revealed considerable differences between the regulation of these two genes.

L2 ANSWER 10 OF 21 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 1997236570 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9083266
TITLE: Dual effect of lysophosphatidic acid on proliferation of glomerular mesangial cells.
AUTHOR: Gaits F; Salles J P; Chap H
CORPORATE SOURCE: Institut Federatif de Recherche en Immunologie Cellulaire et Moleculaire, Universite Paul Sabatier, Toulouse, France.
SOURCE: Kidney international, (1997 Apr) Vol. 51, No. 4, pp. 1022-7.
Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 9 Jul 1997
Last Updated on STN: 6 Feb 1998
Entered Medline: 20 Jun 1997

AB Among the variety of factors able to contribute to mesangial hypertrophy by altering mesangial cell growth, lysophosphatidic acid (LPA) is the focus of increasing attention. It is produced in plasma following platelet activation, as well as by mesangial cells stimulated by secretory phospholipase A2. As mitogenic/antimitogenic properties of LPA are already described in a variety of cells, knowledge of its specific actions on mesangial cells is of potential interest regarding the pathophysiology of glomerulus damage in situ. We tested the effect of LPA on cultured rat mesangial cell growth. At 10 to 20 microM, LPA stimulated thymidine incorporation as well as phosphorylation of mitogen-activated protein kinases (MAP-kinases) p42-p44 in dose- and time-dependent manner, which demonstrated a positive effect on cell proliferation. However, higher concentrations of LPA (100 microM) were unable to stimulate thymidine incorporation and partly inhibited the proliferative effect as well as p42-p44 phosphorylation evoked by serum. Finally, whereas lysophosphatidylcholine (10 to 20 microM) was lytic for mesangial cells, no cell lysis could be detected at the highest concentrations of LPA. Taken together, these results suggest that LPA exerts a dual effect on mesangial cell proliferation, which could be due to activation of distinct specific signaling pathways, in dose-dependent fashion. Specific actions of LPA able to modify mesangial cell proliferation in a positive or negative manner are also likely to influence the pathophysiological processes involved in the progression of glomerulosclerosis in the kidney.

L2 ANSWER 11 OF 21 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 1998063733 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9402141
TITLE: Lysophosphatidic acid and platelet-derived growth factor synergistically stimulate growth of cultured rat mesangial cells.
AUTHOR: Inoue C N; Ko Y H; Guggino W B; Forster H G; Epstein M
CORPORATE SOURCE: Nephrology Section, VA Medical Center, University of Miami School of Medicine, Florida 33125, USA.
SOURCE: Proceedings of the Society for Experimental Biology and Medicine. Society for Experimental Biology and Medicine (New York, N.Y.), (1997 Dec) Vol. 216, No. 3, pp. 370-9.
Journal code: 7505892. ISSN: 0037-9727.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 9 Jan 1998
Last Updated on STN: 9 Jan 1998
Entered Medline: 23 Dec 1997

AB Lysophosphatidic acid (LPA) is a structurally simple, platelet-derived phospholipid, capable of eliciting a variety of physiological responses. We have demonstrated previously that LPA elicited a marked contractile response in rat mesangial cells (Inoue CN, Forster

HG, Epstein M. Circ Res 77:888-896, 1995). In the present study, we examined the potential of this vasoactive substance to induce mesangial cell proliferation. Serum-starved quiescent rat mesangial cells were incubated with either LPA or in combination with platelet-derived growth factor (PDGF). DNA synthesis was assessed by [3H]thymidine incorporation after 24 hr, and cell numbers were determined at 0, 4, and 7 days. LPA- (1 nM-30 microM) stimulated mesangial cell DNA synthesis in a dose-dependent manner. The DNA synthesis stimulated by PDGF (1-100 ng/ml) was characterized by a bell-shaped response curve with a maximum at 40 ng/ml PDGF. The ability of LPA (30 microM) to synergize PDGF was observed over the entire range of PDGF concentrations (1-100 ng/ml). Under optimal concentrations of LPA/PDGF (30 microM40 ng/ml, respectively), mesangial cells displayed a 67-fold increase in [3H]thymidine incorporation, and a 1.9-fold (Day 4) and 2.5-fold (Day 7) increase in cell number as compared with that of quiescent mesangial cells. With an in vitro assay with myelin basic protein as the substrate, both LPA and PDGF induced stimulation of mitogen-activated protein (MAP) kinase activity. In addition, LPA augmented PDGF-induced increase in MAP kinase activity. In summary, these results demonstrate that LPA is mitogenic alone and also acts synergistically in combination with PDGF to promote mesangial cell proliferation. We postulate that these actions of LPA have the potential to play a crucial role in the mitogenic response of mesangial cells seen in a wide array of inflammatory and thrombotic glomerular disorders.

L2 ANSWER 12 OF 21 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 1996027697 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7554142
TITLE: Effects of lysophosphatidic acid, a novel lipid mediator, on cytosolic Ca2+ and contractility in cultured rat mesangial cells.
AUTHOR: Inoue C N; Forster H G; Epstein M
CORPORATE SOURCE: Nephrology Section, Miami VA Medical Center, FL 33125, USA.
SOURCE: Circulation research, (1995 Nov) Vol. 77, No. 5, pp. 888-96.
Journal code: 0047103. ISSN: 0009-7330.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 27 Dec 1995
Last Updated on STN: 3 Feb 1997
Entered Medline: 20 Nov 1995

AB Lysophosphatidic acid (LPA), the smallest and structurally simplest phospholipid, has the potential to modulate cellular signaling in diverse tissues and cell types, including fibroblasts. In the present study, we assessed the effects of LPA on cultured rat glomerular mesangial cells. Quantitative changes of [Ca2+]i in response to LPA were measured in monolayers of mesangial cells loaded with the fluorescent Ca2+ indicator fura 2. LPA (10 nmol/L to 100 mumol/L) increased [Ca2+]i in a dose-dependent manner and evoked inositol trisphosphate formation. LPA (1 mumol/L to 30 mumol/L) also elicited a marked, albeit transient, contractile response in mesangial cells cultured on collagen gel, as assessed by a decrease in cell surface area (CSA). The contraction persisted for 5 minutes (CSA decreased by 31%), whereupon the mesangial cells gradually relaxed with a consequent increase in CSA. Pretreatment of mesangial cells with isradipine (1 mumol/L), a

dihydropyridine-sensitive Ca2+ channel blocker, completely blocked LPA-induced contraction. Isradipine also decreased resting [Ca2+]i levels as well as the peak and the subsequently sustained [Ca2+]i levels induced by LPA, suggesting that the contractile effects of LPA are dependent on Ca2+ entry through voltage-gated Ca2+ channels. Finally, LPA stimulated an increase in both prostaglandin E2 synthesis and cAMP accumulation, indicating that these mediators may modulate the contractile effects of LPA. Our study is the first demonstration that exogenous LPA induces mesangial cell contraction and suggests that the contraction is mediated by mobilization of intracellular Ca2+ by activation of the phosphoinositide cascade as well as by promotion of Ca2+ entry across the plasma membrane.

L2 ANSWER 13 OF 21 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 1993158778 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8430826
TITLE: Role of mesangial cell in glomerular response to volume and angiotensin II.
AUTHOR: Blantz R C; Gabbai F B; Tucker B J; Yamamoto T; Wilson C B
CORPORATE SOURCE: Division of Nephrology-Hypertension, University of California San Diego, La Jolla 92093.
CONTRACT NUMBER: DK-28602 (United States NIDDK)
DK-40251 (United States NIDDK)
SOURCE: The American journal of physiology, (1993 Jan) Vol. 264, No. 1 Pt 2, pp. F158-65. Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 26 Mar 1993
Last Updated on STN: 26 Mar 1993
Entered Medline: 5 Mar 1993

AB We have examined the physiological role of the mesangial cell in the regulation of glomerular hemodynamics utilizing mesangial cell lysis by the administration of antithymocyte antibody serum (ATS) 24 h before micropuncture evaluation. Plasma volume expansion (PVE) in normal NaCl-depleted rats increased single-nephron glomerular filtration rate (SNGFR) by 30% because of increases in single-nephron plasma flow (SNPF), whereas glomerular capillary hydrostatic pressure (PG) remained constant. SNGFR did not increase with PVE in NaCl-depleted ATS rats despite increases in SNPF, and PG increased significantly (51 +/- 2 to 67 +/- 3 mmHg) because of afferent arteriolar dilation, whereas efferent resistance remained elevated. Angiotensin II (ANG II) infusion in normal rats decreased SNGFR because of reductions in SNPF and the glomerular ultrafiltration coefficient (LpA), whereas the hydrostatic pressure gradient (delta P) increased. In ATS rats ANG II infusion did not change SNGFR, LpA, or delta P. These in vivo studies suggest that the mesangial cell plays an important role in the regulation of LpA, efferent arteriolar resistance, and the regulation of PG, whereas this cell exerts little effect on the afferent arteriole.

L2 ANSWER 14 OF 21 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 1986293057 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3526892
TITLE: Effect of immunoglobulin depositions of glomerular sialic acids in patients with IgA nephropathy.
AUTHOR: Tomino Y; Sakai H; Miura M; Suga T; Yagame M; Endoh M; Nomoto Y

SOURCE: American journal of nephrology, (1986) Vol. 6, No. 3, pp. 187-92. Journal code: 8109361. ISSN: 0250-8095.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198609
ENTRY DATE: Entered STN: 21 Mar 1990 Last Updated on STN: 21 Mar 1990 Entered Medline: 16 Sep 1986

AB A study of double immunofluorescence-staining of immunoglobulins and sialic acids in the glomeruli from patients with IgA nephropathy is described. Renal biopsy specimens from patients with IgA nephropathy were stained with rhodamine-labeled antihuman IgA, IgG or IgM antisera and then stained with FITC-labeled Limulus polyphemus (LPA), Tricum vulgaris (WGA) or antihuman C3 antisera. Marked positive stainings of IgA and C3 and positive binding of LPA or WGA were observed in the glomerular mesangial areas from patients with IgA nephropathy. LPA or WGA were not bound with glomerular capillary walls from patients with moderate and advanced stages of IgA nephropathy, although depositions of IgA and C3 were markedly observed in such walls. There was a significant inverse correlation between the deposition of IgA and the binding of LPA or WGA in glomerular capillary walls obtained from these patients with IgA nephropathy. The levels of proteinuria from patients with moderate and advanced stages of IgA nephropathy were significantly higher than those with minimal and slight stages of such disease. It is suggested that the decrease of sialic acids in glomerular capillary walls might be due to a deposition of IgA in some patients with IgA nephropathy. It is concluded that high levels of proteinuria might be due to the decrease of sialic acids in glomerular capillary walls from patients with moderate and advanced stages of IgA nephropathy.

L2 ANSWER 15 OF 21 MEDLINE on STN
ACCESSION NUMBER: 1987267592 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2886045
TITLE: The glomerular and tubular actions of angiotensin II.
AUTHOR: Blantz R C
CONTRACT NUMBER: AM28602 (United States NIADDK) HL25457 (United States NHLBI)
SOURCE: American journal of kidney diseases : the official journal of the National Kidney Foundation, (1987 Jul) Vol. 10, No. 1 Suppl 1, pp. 2-6. Ref: 39 Journal code: 8110075. ISSN: 0272-6386.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198708
ENTRY DATE: Entered STN: 5 Mar 1990 Last Updated on STN: 3 Feb 1997 Entered Medline: 13 Aug 1987

AB Evidence has accumulated that angiotensin II (AII) exerts multiple influences upon renal function through effects on vascular, glomerular, and tubular structures. Infusion of AII alters glomerular ultrafiltration by decreasing nephron plasma flow, increasing glomerular capillary hydrostatic pressure (PG) and the hydrostatic pressure gradient (delta P) due to increases in both afferent and efferent arteriolar vascular

resistance, and effecting a reduction in the glomerular ultrafiltration coefficient (LpA), the product of glomerular membrane hydraulic conductivity and effective surface area for ultrafiltration. Spontaneous increases in intrarenal AII generation, such as observed in chronic NaCl depletion, also produce reductions in nephron plasma flow, increases in delta P, and major reductions in LpA. Angiotensin-converting enzyme inhibitor and saralasin administration prevent these alterations in plasma flow, delta P, and LpA. These AII-induced alterations in LpA may be mediated by AII effects upon the glomerular mesangial cell since AII receptors are expressed and this cell contracts in vitro in the presence of AII. Multiple studies have shown a positive effect of AII (approximately 10(-11) mol/L) on proximal tubular reabsorption, an effect independent of AII effects on peritubular physical factors. These AII effects upon the proximal tubule are clearly independent of interaction with adrenergic influences. AII also influences other mesangial cell functions such as uptake of macromolecules from the circulation. AII also exerts effects by influencing the functional expression of renal adrenergic activity, as demonstrated by studies with renal nerve stimulation in the presence and absence of angiotensin-converting enzyme inhibitor and saralasin. Inhibition of AII activity also clearly suppresses tubuloglomerular activity and the PG response to alterations in distal tubular flow rates.(ABSTRACT TRUNCATED AT 250 WORDS)

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pd<=20031211
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L1          23 ((LYSOPHOSPHATIDIC ACID) OR LPA) (P) RECEPTOR (P) (DETECTION OR
               KIT) AND PD<=20031211

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L2           10 DUP REM L1 (13 DUPLICATES REMOVED)
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                ANSWERS '8-10' FROM FILE CAPLUS

=> D Ibib Abs L2 1-10

L2   ANSWER 1 OF 10     MEDLINE on STN                  DUPLICATE 1
ACCESSION NUMBER:   2002047383     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11775454
TITLE:              Critical role of lysophospholipids in the pathophysiology,
                    diagnosis, and management of ovarian cancer.
AUTHOR:             Mills Gordon B; Eder Astrid; Fang Xianjun; Hasegawa Yutaka;
                    Mao Muling; Lu Yiling; Tanyi Janos; Tabassam Fazal Haq;
                    Wiener Jon; Lapushin Ruth; Yu Shiangxing; Parrott Jeff A;
                    Compton Tim; Tribley Walter; Fishman David; Stack M Sharon;
                    Gaudette Douglas; Jaffe Robert; Furui Tatsuro; Aoki Junken;
                    Erickson James R
CORPORATE SOURCE:   Department of Molecular Therapeutics, MD Anderson Cancer
                    Center, 1515 Holcombe Boulevard, Houston, Texas 77030, USA.
CONTRACT NUMBER:    P01 CA64602 (United States NCI)
SOURCE:             Cancer treatment and research, (2002) Vol. 107,
                    pp. 259-83.  Ref: 89
                    Journal code: 8008541. ISSN: 0927-3042.
PUB. COUNTRY:       Netherlands
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, NON-U.S. GOV'T)
                    (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
                    General Review; (REVIEW)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200204
ENTRY DATE:         Entered STN: 25 Jan 2002
                    Last Updated on STN: 24 Apr 2002
                    Entered Medline: 23 Apr 2002
AB   Lysophosphatidic acid (LPA), the simplest of
     all phospholipids, exhibits pleiomorphic functions in multiple cell
     lineages.  The effects of LPA appear to be mediated by binding
     of LPA to specific members of the endothelial differentiation
     gene (Edg) family of G protein-coupled receptors (GPCR).  Edg 2,
     Edg4, and Edg7 are high affinity receptors for LPA,
     and Edg1 may be a low affinity receptor for LPA.
     PSP24 has been shown to be responsive to LPA in Xenopus oocytes,
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however, its role in mammalian cells is unclear. The specific biochemical events initiated by the different Edg receptors, as well as the biological outcomes of activation of the individual receptors, are only beginning to be determined. LPA levels are consistently elevated in the plasma and ascites of ovarian cancer patients, but not in most other epithelial tumors, with the exception of cervix and endometrium, suggesting that LPA may be of particular importance in the pathophysiology of ovarian cancer. In support of this concept, ovarian cancer cells constitutively and inducibly produce high levels of LPA and demonstrate markedly different responses to LPA than normal ovarian surface epithelium. Edg4 and Edg7 levels are consistently increased in malignant ovarian epithelial cells contributing to the aberrant response of ovarian cancer cells to LPA. Edg2 may represent a negative regulatory LPA receptor inducing apoptosis in ovarian cancer cells. Thus, increased levels of LPA, altered receptor expression and altered responses to LPA may contribute to the initiation, progression or outcome of ovarian cancer. Over 40% of known drugs target GPCR, making LPA receptors attractive targets for molecular therapeutics. Indeed, using the structure-function relationship of LPA in model systems, we have identified selective Edg2 anatgonists, as well as Edg4 and Edg7 agonists. These lead compounds are being assessed in preclinical model systems. Understanding the mechanisms regulating LPA production, metabolism and function could lead to improved methods for early detection and to new targets for therapy in ovarian cancer.

L2 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001682485 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11728312
TITLE: Regulating c-Ras function. cholesterol depletion affects caveolin association, GTP loading, and signaling.
AUTHOR: Kranenburg O; Verlaan I; Moolenaar W H
CORPORATE SOURCE: Division of Cellular Biochemistry, The Netherlands Cancer Institute, Center for Biomedical Genetics, Plesmanlaan 121, 1066CX Amsterdam, The Netherlands.
SOURCE: Current biology : CB, (2001 Nov 27) Vol. 11, No. 23, pp. 1880-4.
Journal code: 9107782. ISSN: 0960-9822.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 3 Dec 2001
Last Updated on STN: 14 Feb 2002
Entered Medline: 13 Feb 2002

AB Cholesterol-rich and caveolin-containing microdomains of the plasma membrane, termed "caveolae," have been implicated in signal transduction. However, the role of caveolae in regulating the Ras-MAP kinase cascade is incompletely understood. The mammalian Ras isoforms (H, N, and K) use different membrane anchors to attach to the plasma membrane and thereby may localize to functionally distinct microdomains, which might explain isoform-specific signaling. Here, we show that, in Cos epithelial cells, endogenous K-Ras colocalizes largely with caveolin, whereas N-Ras localizes to both caveolar and noncaveolar subdomains; H-Ras localization was below detection limits. We find that epidermal growth factor (EGF) activates N-Ras but fails to activate K-Ras in these cells. Extraction of cholesterol with methyl-beta-cyclodextrin disrupts complex formation between caveolin and K- and N-Ras and, strikingly, enables EGF to activate both K-Ras and N-Ras. While cholesterol depletion enhances

GTP-loading on total c-Ras, activation of the downstream MEK-MAP kinase cascade by EGF and lysophosphatidic acid but not that by phorbol ester is inhibited. Thus, plasma membrane cholesterol is essential for negative regulation of c-Ras isoforms (complexed to caveolin), as well as for mitogenic signaling downstream of receptor-activated c-Ras.

L2 ANSWER 3 OF 10 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2000384072 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10891442
TITLE: Sphingosine-1-phosphate and lysophosphatidic acid trigger invasion of primitive hematopoietic cells into stromal cell layers.
AUTHOR: Yanai N; Matsui N; Furusawa T; Okubo T; Obinata M
CORPORATE SOURCE: Department of Cell Biology, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan.
SOURCE: Blood, (2000 Jul 1) Vol. 96, No. 1, pp. 139-44. Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 18 Aug 2000
Last Updated on STN: 18 Aug 2000
Entered Medline: 10 Aug 2000

AB A new primitive hematopoietic cell line (THS119), exhibiting Lin(-)/Sca-1(+)/c-Kit(+) a surface phenotype, grew and survived underneath stromal cells (TBR59). The ability of the THS119 cells to invade these stromal cell layers was dependent on the inclusion of serum in the culture medium. This was apparently due to a requirement for lipids contained in serum. Their invasion of the stromal cell layers in serum-free cultures could be triggered by addition of sphingosine-1-phosphate (S1P) or lysophosphatidic acid (LPA) and was dependent on both Rho- and Ras-signaling pathways. Between the 2 possible receptors of S1P and LPA, edg-1 and edg-2, expression of edg-2 only was found to be correlated with immaturity and/or invasive activity of the primitive hematopoietic cells. These results suggest the importance of specific lipids and their specific receptors on the invasive activity of primitive hematopoietic cells in the hematopoietic microenvironment.

L2 ANSWER 4 OF 10 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1999287728 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10359601
TITLE: Activation of RhoA by lysophosphatidic acid and Galpha12/13 subunits in neuronal cells: induction of neurite retraction.
AUTHOR: Kranenburg O; Poland M; van Horck F P; Drechsel D; Hall A; Moolenaar W H
CORPORATE SOURCE: The Netherlands Cancer Institute, Division of Cellular Biochemistry, 1066 CX Amsterdam, The Netherlands.
SOURCE: Molecular biology of the cell, (1999 Jun) Vol. 10, No. 6, pp. 1851-7. Journal code: 9201390. ISSN: 1059-1524.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907

ENTRY DATE: Entered STN: 6 Aug 1999
Last Updated on STN: 20 Apr 2002
Entered Medline: 29 Jul 1999

AB Neuronal cells undergo rapid growth cone collapse, neurite retraction, and cell rounding in response to certain G protein-coupled receptor agonists such as lysophosphatidic acid (LPA). These shape changes are driven by Rho-mediated contraction of the actomyosin-based cytoskeleton. To date, however, detection of Rho activation has been hampered by the lack of a suitable assay. Furthermore, the nature of the G protein(s) mediating LPA -induced neurite retraction remains unknown. We have developed a Rho activation assay that is based on the specific binding of active RhoA to its downstream effector Rho-kinase (ROK). A fusion protein of GST and the Rho-binding domain of ROK pulls down activated but not inactive RhoA from cell lysates. Using GST-ROK, we show that in N1E-115 neuronal cells LPA activates endogenous RhoA within 30 s, concomitant with growth cone collapse. Maximal activation occurs after 3 min when neurite retraction is complete and the actin cytoskeleton is fully contracted. LPA-induced RhoA activation is completely inhibited by tyrosine kinase inhibitors (tyrphostin 47 and genistein). Activated Galpha12 and Galpha13 subunits mimic LPA both in activating RhoA and in inducing RhoA-mediated cytoskeletal contraction, thereby preventing neurite outgrowth. We conclude that in neuronal cells, LPA activates RhoA to induce growth cone collapse and neurite retraction through a G12/13-initiated pathway that involves protein-tyrosine kinase activity.

L2 ANSWER 5 OF 10 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 1998338028 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9671791
TITLE: Ligand-independent activation of platelet-derived growth factor receptor is a necessary intermediate in lysophosphatidic, acid-stimulated mitogenic activity in L cells.
AUTHOR: Herrlich A; Daub H; Knebel A; Herrlich P; Ullrich A; Schultz G; Gudermann T
CORPORATE SOURCE: Institut fur Pharmakologie, Freie Universitat Berlin, Thielallee 67-73, 14195 Berlin, Germany.. andreas.herrlich@igenfzk.de
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1998 Jul 21) Vol. 95, No. 15, pp. 8985-90.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 28 Aug 1998
Last Updated on STN: 3 Mar 2000
Entered Medline: 20 Aug 1998

AB Growth factor-derived mitogenic signals from the cell surface are transmitted to the nucleus via receptor tyrosine kinases (RTKs), the adaptor proteins Shc and Grb2, and a Ras-dependent protein kinase cascade that activates the extracellular signal regulated kinase (ERK) subfamily of mitogen-activated protein kinases. ERKs also are activated by hormones that stimulate G protein-coupled receptors (GPCRs). We report here that, in agreement with previous data, the epidermal growth factor receptor (EGFR) is a signaling intermediate in ERK activation by GPCRs. Of import, we show that cross-talk between two classes of surface receptors, RTKs and GPCRs, is a general

feature. Lysophosphatidic acid not only induces ligand-independent tyrosine autophosphorylation of EGFR but also of platelet-derived growth factor beta receptor (PDGF-beta-R) as shown by detection of tyrosine phosphorylation and by the use of specific inhibitors of RTKs. The cross-talk appears to be cell type-specific: In L cells that lack EGFR, lysophosphatidic acid-induced Shc and ERK activation is prevented completely by specific inhibition of PDGFR, whereas in COS-7 cells expressing only EGFR, the pathway via EGFR is chosen. In Rat-1 cells, however, that express both EGFR and PDGFR, the EGFR pathway dominates.

L2 ANSWER 6 OF 10 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 1998300465 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9636836
TITLE: Malignant effusions contain lysophosphatidic acid (LPA)-like activity.
AUTHOR: Westermann A M; Havik E; Postma F R; Beijnen J H; Dalesio O; Moolenaar W H; Rodenhuis S
CORPORATE SOURCE: Department of Medical Oncology, The Netherlands Cancer Institute, Amsterdam, The Netherlands.. annie@nki.nl
SOURCE: Annals of oncology : official journal of the European Society for Medical Oncology / ESMO, (1998 Apr) Vol. 9, No. 4, pp. 437-42. Journal code: 9007735. ISSN: 0923-7534.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 17 Sep 1998 Last Updated on STN: 17 Sep 1998 Entered Medline: 10 Sep 1998
AB BACKGROUND: Lysophosphatidic acid (LPA) and sphingosine-1-phosphate (S1P) are bioactive phospholipids with mitogenic and growth factor-like activities that act via specific cell-surface receptors present in many normal and transformed cell types. LPA has recently been implicated as a growth factor present in ascites of ovarian cancer patients. The presence of LPA-like activity and the hypothesis that levels of this bioactivity in effusions of ovarian cancer patients are higher than those in effusions of other cancer patients was studied. MATERIALS AND METHODS: A neurite retraction bioassay in a neuroblastoma cell line previously developed for in vitro detection of LPA activity on cell lines was employed and bioactivity was expressed in virtual LPA-equivalent levels. LPA-equivalent levels were tested in effusions of 62 patients with a range of malignancies, including 13 ovarian cancer patients. Biochemical and clinical parameters were evaluated for correlations with LPA-equivalent levels. RESULTS: Average LPA-equivalent levels were 50.2 microns (range 5.4-200) for all patients, and 94.5 microns (range 15-200) for ovarian cancer patients (P = 0.004). There were no additional independent significant correlations between LPA-equivalent levels in effusions and a range of other biochemical and clinical characteristics. CONCLUSION: These data suggest a role for LPA-like lipids in the peritoneal spread of ovarian cancer and possibly that of other predominantly intraperitoneal malignancies.

L2 ANSWER 7 OF 10 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:55169 BIOSIS
DOCUMENT NUMBER: PREV200300055169
TITLE: Methods for detecting compounds which modulate the activity

of an LPA receptor.
AUTHOR(S): Erickson, James [Inventor, Reprint Author]; Goddard, J. Graham [Inventor]; Kiefer, Michael [Inventor]
CORPORATE SOURCE: El Cerrito, CA, USA
ASSIGNEE: Atairgin Technologies, Inc.
PATENT INFORMATION: US 6485922 20021126
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov 26 2002) Vol. 1264, No. 4. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Jan 2003
Last Updated on STN: 22 Jan 2003
AB The present invention provides novel methods for identifying and characterizing compounds that modulate the activity of an LPA receptor.

L2 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:293827 CAPLUS
DOCUMENT NUMBER: 136:321269
TITLE: Human testis phosphatidic acid-specific phospholipase A1 cDNAs and uses in drug screening, diagnosis, and therapy
INVENTOR(S): Arai, Hiroyuki; Aoki, Junken
PATENT ASSIGNEE(S): Mochida Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002031131	A1	20020418	WO 2001-JP7106	20010820 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001078773	A	20020422	AU 2001-78773	20010820 <--
CA 2425845	A1	20030411	CA 2001-2425845	20010820 <--
EP 1329501	A1	20030723	EP 2001-956958	20010820 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 20040253221	A1	20041216	US 2003-398869	20030818
PRIORITY APPLN. INFO.:			JP 2000-311015 A	20001011
			WO 2001-JP7106 W	20010820

AB A novel phospholipase A1 (PLA1) from human having a substrate specificity to phosphatidic acid (PA); a cDNA encoding it; recombinant expression; antibodies; and use in drug screening, diagnosis, and therapy; are disclosed. Cloning and expression of phosphatidic acid-specific phospholipase A1 cDNAs is reported. The open reading frames encoded an 460 and 481-amino acid proteins. The sequence included a region similar to a lipase consensus sequence containing the putative catalytic triad and also included a potential asparagine glycosylation sites. Expression in Sf9 cells resulted in detection of phosphatidic acid phospholipase A1 activity. Northern blot anal. revealed the highest

overall expression levels in testis. It catalyzes hydrolysis of PA to produce lysophosphatidic acid (LPA). Its role in 2-acyl LPA specific receptor EDG7 mediated signaling was observed

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:123078 CAPLUS
DOCUMENT NUMBER: 136:162384
TITLE: Haplotypes and genotyping of the human EDG4 gene encoding endothelial differentiation lysophosphatidic acid G protein-coupled receptor 4
INVENTOR(S): Kazemi, Amir; Koshy, Beena; Sanchis, Angela
PATENT ASSIGNEE(S): Genaissance Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012342	A2	20020214	WO 2001-US24649	20010806 <--
WO 2002012342	A3	20030828		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001084732	A	20020218	AU 2001-84732	20010806 <--
PRIORITY APPLN. INFO.:			US 2000-223177P	P 20000804
			WO 2001-US24649	W 20010806

AB Novel single nucleotide polymorphisms in the human endothelial differentiation lysophosphatidic acid G protein-coupled receptor 4 (EDG4) gene are described. Eight novel polymorphic sites and 8 isogenes are discovered by characterizing the EDG4 gene found in genomic DNAs isolated from an Index Repository that contains immortalized cell lines from one chimpanzee and 93 human individuals self-identified as belonging to one of the four major population groups. To the extent possible, the members of this reference population were organized into population subgroups by the self-identified ethnogeog. origin of their four grandparents. Three polymorphic sites are identified in the coding region of EDG4, resulting in a single polymorphic position in the protein. In addition, various genotypes, haplotypes and haplotype pairs for the EDG4 gene that exist in the population are described. Compns. and methods for haplotyping and/or genotyping the EDG4 gene in an individual are also disclosed. Polynucleotides containing one or more of the EDG4 polymorphisms disclosed herein are also described.

L2 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:31636 CAPLUS
DOCUMENT NUMBER: 136:81954
TITLE: Human phosphatidic acid-preferring phospholipase A1
INVENTOR(S): Inoue, Keizo; Arai, Hiroyuki; Aoki, Junken
PATENT ASSIGNEE(S): Mochida Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002762	A1	20020110	WO 2000-JP4441	20000703 <--
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2416191	A1	20020110	CA 2000-2416191	20000703 <--
EP 1298205	A1	20030402	EP 2000-942470	20000703 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 20070202520	A1	20070830	US 2007-652080	20070111
PRIORITY APPLN. INFO.:			WO 2000-JP4441 W	20000703
			US 2003-311974 B1	20030430

AB A novel phospholipase A1 (PLA1) from human having a substrate specificity to phosphatidic acid (PA); a cDNA encoding it; recombinant expression; antibodies; and use in drug screening, diagnosis, and therapy; are disclosed. The mol. cloning and expression of a phosphatidic acid-specific phospholipase A1 (colon lipase) cDNA is reported. The open reading frame encoded an 451-amino acid protein. The sequence included a region similar to a lipase consensus sequence containing the putative catalytic triad and also included a potential glycosylation sites. Expression in Sf9 cells resulted in detection of phosphatidic acid phospholipase A1 activity mostly in membrane fraction. Northern blot anal. revealed the highest overall expression levels in lung, kidney, spleen, prostate, testis, ovary, and rectum. It catalyzes hydrolysis of PA to produce 2-acyl lysophosphatidic acid (LPA) and has affinity for heparin. Its role in 2-acyl LPA specific receptor EDG7 mediated signaling was observed
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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STN INTERNATIONAL SESSION SUSPENDED AT 14:06:13 ON 09 OCT 2008

Connecting via Winsock to STN

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LOGINID:SSPTAEGS1646

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
AT 14:58:08 ON 09 OCT 2008
FILE 'MEDLINE' ENTERED AT 14:58:08 ON 09 OCT 2008
FILE 'BIOSIS' ENTERED AT 14:58:08 ON 09 OCT 2008
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FILE 'CAPLUS' ENTERED AT 14:58:08 ON 09 OCT 2008
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)
FILE 'EMBASE' ENTERED AT 14:58:08 ON 09 OCT 2008

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	49.54	49.75

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.40	-2.40

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     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 13:47:30 ON 09 OCT 2008
L1           23 S ((LYSOPHOSPHATIDIC ACID) OR LPA) (P)RECEPTOR (P) (DETECTION O
L2           10 DUP REM L1 (13 DUPLICATES REMOVED)

=> S ((LYSOPHOSPHATIDIC ACID) OR LPA) (S) kit AND pd<=20031211
   1 FILES SEARCHED...
L3           15 ((LYSOPHOSPHATIDIC ACID) OR LPA) (S) KIT AND PD<=20031211

=> Dup REm L3
PROCESSING COMPLETED FOR L3
L4           11 DUP REM L3 (4 DUPLICATES REMOVED)
                ANSWERS '1-2' FROM FILE MEDLINE
                ANSWERS '3-4' FROM FILE BIOSIS
                ANSWERS '5-11' FROM FILE CAPLUS

=> D IBIB Abs L4 1-11

L4   ANSWER 1 OF 11     MEDLINE on STN                  DUPLICATE 1
ACCESSION NUMBER:   2003561612     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 14649475
TITLE:              Bacterial antigen detection test in meningitis.
AUTHOR:             Das B K; Gurubacharya Rajesh Lal; Mohapatra T M; Mishra O P
CORPORATE SOURCE:   Department of Pediatrics, Institute of Medical Sciences,
                    Banaras Hindu University, Varanasi, India.
SOURCE:             Indian journal of pediatrics, (2003 Oct) Vol. 70,
                    No. 10, pp. 799-801.
                    Journal code: 0417442. ISSN: 0019-5456.
PUB. COUNTRY:       India
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200401
ENTRY DATE:         Entered STN: 16 Dec 2003
                    Last Updated on STN: 30 Jan 2004
                    Entered Medline: 29 Jan 2004
AB   OBJECTIVE: To evaluate the role of bacterial antigen detection test in
     cerebrospinal fluid (CSF) for a rapid etiological diagnosis of bacterial
     meningitis.  METHODS: The study included 36 cases of bacterial meningitis
     and 14 controls.  Latex particle agglutination test (LPA test)
     for detection of bacterial antigen was done in the CSF using slidex
     meningitis kit (Biomeriux, France).  RESULTS: Using LPA test, an
     etiological diagnosis could be made in 83% cases of bacterial meningitis.
     In contrast, CSF Gram stain and culture showed 36% and 6% positivity,
     respectively.  The sensitivity and specificity of LPA test were 83% and
     100%, respectively.  The common etiological organisms were S. pneumoniae,
     H. influenzae type b and N. meningitidis A.  S. pneumoniae was encountered
     in all age groups while H. influenzae type b was found only below one year
     of age.  CONCLUSIONS: LPA test is a rapid and superior diagnostic tool as
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compared to CSF Gram stain and culture. The study recommends LPA test as an adjunct laboratory test for rapid etiological diagnosis of bacterial meningitis for prompt institution of proper antibiotics.

L4 ANSWER 2 OF 11 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1993107274 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8417036
TITLE: Comparison of two antigen assays for rapid intrapartum detection of vaginal group B streptococcal colonization.
AUTHOR: Green M; Dashefsky B; Wald E R; Laifer S; Harger J; Guthrie R
CORPORATE SOURCE: University of Pittsburgh School of Medicine, Department of Pediatrics, Pennsylvania.
SOURCE: Journal of clinical microbiology, (1993 Jan) Vol. 31, No. 1, pp. 78-82.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199301
ENTRY DATE: Entered STN: 12 Feb 1993
Last Updated on STN: 12 Feb 1993
Entered Medline: 22 Jan 1993
AB As part of a clinical investigation evaluating the efficacy of intrapartum antigen detection for screening for heavy vaginal colonization with group B streptococci (GBS), we compared the performance of modified Bactigen and Directigen GBS latex particle agglutination (LPA) kits
. Paired vaginal swabs obtained from women in labor were rapidly transported to the laboratory and used for culturing (both swabs) and LPA testing (one swab by each method). GBS growth was estimated semiquantitatively and further designated as light or heavy growth. Performance specifications for each method were determined by comparing LPA and culture results from the same swab. A total of 4,251 paired swabs were evaluated during the study period. The performance specifications for detecting GBS growth of any degree for Bactigen and Directigen, respectively, were as follows: sensitivity, 20 and 24%; specificity, 99 and 99%. The performance specifications for heavy colonization for Bactigen and Directigen, respectively, were as follows: sensitivity, 57 and 62%; specificity, 99 and 99%. Neither LPA kit was a sensitive indicator of vaginal colonization with GBS or neonatal infection.

L4 ANSWER 3 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:6582 BIOSIS
DOCUMENT NUMBER: PREV200300006582
TITLE: Recombinant lysophosphatidic acid phosphatase.
AUTHOR(S): Takenawa, Tadaomi [Inventor, Reprint Author]; Hiroyama, Masami [Inventor]; Kishimoto, Tatsuya [Inventor]; Yamaguchi, Masahiro [Inventor]; Toyosato, Mitsuyoshi [Inventor]; Mizuno, Kouji [Inventor]
CORPORATE SOURCE: Tokyo, Japan
ASSIGNEE: Azwell Inc., Osaka, Japan
PATENT INFORMATION: US 6472193 20021029
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct 29 2002) Vol. 1263, No. 5. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English

ENTRY DATE: Entered STN: 18 Dec 2002
Last Updated on STN: 18 Dec 2002

AB An object of the present invention is to provide a recombinant LPA phosphates capable of specifically hydrolyzing LPA, which is useful for elucidation of the metabolic pathway of LPA, and also for diagnosis and treatment of various diseases with which LPA is associated. The present invention also provides for a method capable of simply and inexpensively determining LPA associated with various diseases. The present invention also provides for a kit for determination suitable for the method. The present invention has succeeded in purifying the LPA phosphatase using bovine brain as a raw material, and further in cloning human LPA phosphatase gene. The present invention specifically relates to a DNA encoding a peptide comprising the amino acid sequence of SEQ ID NO:1; a DNA comprising the nucleotide sequence of SEQ ID NO:2; a protein encoded by the DNA; and expression vector carrying the DNA; a transformant harboring the expression vector; a method for producing a recombinant lysophosphatidic acid phosphatase by the transformant; a method for determination of LPA by the protein; a determination reagent for LPA by the protein; a kit for diagnosis, comprising the reagent for determination, and the like.

L4 ANSWER 4 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:369768 BIOSIS
DOCUMENT NUMBER: PREV200200369768
TITLE: Dyslipidemia among type-2 diabetic and hypertensive Nepalese: Implication of measuring serum lipoprotein(a).
AUTHOR(S): Lamsal, Madhab [Reprint author]; Baral, Nirmal [Reprint author]; Sharma, Sanjeeb K.
CORPORATE SOURCE: Department of Biochemistry, BP.Koirala Institute of Health Sciences, Ghopa, Dharan, Sunsari, 18, Nepal
SOURCE: FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A908-A909. print.
Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Jul 2002
Last Updated on STN: 3 Jul 2002

AB Dyslipidemia along with increased lipoprotein(a)(Lpa) among the type-2 diabetics(DM) and hypertensive(HTN) are of great health concern for the higher prevalence of coronary heart disease(CHD) as compared to non-diabetic, normotensive subjects. Although data are insufficient, CHD is speculatively higher among Nepalese. 225 recently diagoned cases(DM=80,HTN=97,DM+HTN=48) and 112 healthy controls from hill and plain castes were included in this study. Serum total cholesterol(TC), triglyceride(TG), HDL-cholesterol(HDL) were estimated using automated analyser. LDL-cholesterol(LDL) was calculated using Friedewald formula. LPa level was determined by ELISA kits from Innogenetics,Ghent,Belgium. Statistical analysis was done using SPSS.6 package. Significantly raised levels in TC(mg/dl) and LDL(mg/dl) were found among the DM females (hill 206+-39.04 and 136.3+-34.14; plain 203.23+-35.02 and 135.4+-32.33 respectively) as compared to the controls (136+-23.01 and 76.3+-24.01). The mean Lpa level was higher in patient groups(>36mg/dl,P<0.05) as compared to he control(22.5 mg/dl) showing higher risk of CHD in these categories.

L4 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:301221 CAPLUS
DOCUMENT NUMBER: 138:316758

TITLE: Human plasma lysophospholipase D, a lysophosphatidic acid-producing enzyme, as autotaxin, a multifunctional phosphodiesterase, and use in diagnosis, therapy, and drug screening
INVENTOR(S): Tokumura, Akira; Majima, Eiji
PATENT ASSIGNEE(S): Apro Life Science Institute, Inc., Japan
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003031615	A1	20030417	WO 2002-JP10342	20021003 <--
W: AE, AG, AL, AM, AU, AZ, BA, BB, BR, BY, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, RU, SG, SI, TJ, TM, TN, TT, UA, US, UZ, VC, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002362630	A1	20030422	AU 2002-362630	20021003 <--
PRIORITY APPLN. INFO.:			JP 2001-309181 A	20011004
			JP 2002-241043 A	20020821
			WO 2002-JP10342 W	20021003

AB Human plasma lysophospholipase D, previously known as autotaxin, and use in screening its inhibitors for diagnosis of cancer, male reproductive disorders, female reproductive disorders, arteriosclerosis, and pregnancy toxemia (gestational toxicosis), are disclosed. Kits for diagnosis or drug screening are claimed. Use of antibodies as inhibitors is claimed. ATP, p-nitrophenyl 5'-thymidine phosphate. The authors purified human plasma lysophospholipase D that produces physiol. active lysophosphatidic acid and showed that it is a soluble form of autotaxin, an ecto-nucleotide pyrophosphatase/phosphodiesterase, originally found as a tumor cell motility-stimulating factor. Its lower Km value for a lysophosphatidylcholine than that for a synthetic substrate of nucleotide suggests that lysophosphatidylcholine is a more likely physiol. substrate for autotaxin and that its predicted physiol. and pathophysiol. functions could be mediated by its activity to produce lysophosphate acid, an intercellular mediator. Recombinant autotaxin was found to have lysophospholipase D activity; its substrate specificity and metal ion requirement were the same as those of the purified plasma enzyme. The activity of lysophospholipase D for exogenous lysophosphatidylcholine in human serum was found to increase in normal pregnant women at the third trimester of pregnancy and to a higher extent in patients in threatened preterm delivery, suggesting its roles in induction of parturition.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:123078 CAPLUS
DOCUMENT NUMBER: 136:162384
TITLE: Haplotypes and genotyping of the human EDG4 gene encoding endothelial differentiation lysophosphatidic acid G protein-coupled receptor 4
INVENTOR(S): Kazemi, Amir; Koshy, Beena; Sanchis, Angela
PATENT ASSIGNEE(S): Genaissance Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012342	A2	20020214	WO 2001-US24649	20010806 <--
WO 2002012342	A3	20030828		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001084732	A	20020218	AU 2001-84732	20010806 <--
PRIORITY APPLN. INFO.:			US 2000-223177P	P 20000804
			WO 2001-US24649	W 20010806

AB Novel single nucleotide polymorphisms in the human endothelial differentiation lysophosphatidic acid G protein-coupled receptor 4 (EDG4) gene are described. Eight novel polymorphic sites and 8 isogenes are discovered by characterizing the EDG4 gene found in genomic DNAs isolated from an Index Repository that contains immortalized cell lines from one chimpanzee and 93 human individuals self-identified as belonging to one of the four major population groups. To the extent possible, the members of this reference population were organized into population subgroups by the self-identified ethnogeog. origin of their four grandparents. Three polymorphic sites are identified in the coding region of EDG4, resulting in a single polymorphic position in the protein. In addition, various genotypes, haplotypes and haplotype pairs for the EDG4 gene that exist in the population are described. Compns. and methods for haplotyping and/or genotyping the EDG4 gene in an individual are also disclosed. Polynucleotides containing one or more of the EDG4 polymorphisms disclosed herein are also described.

L4 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:338752 CAPLUS
DOCUMENT NUMBER: 134:337920
TITLE: Improved automated LPA assay and methods of detecting cancer
INVENTOR(S): Russell, John C.; Granados, Edward N.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032916	A2	20010510	WO 2000-US30280	20001102 <--
WO 2001032916	A3	20020711		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,

ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2389832 A1 20010510 CA 2000-2389832 20001102 <--
EP 1238099 A2 20020911 EP 2000-976865 20001102 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003530081 T 20031014 JP 2001-535596 20001102 <--
PRIORITY APPLN. INFO.: US 1999-163534P P 19991104
WO 2000-US30280 W 20001102

AB The present invention relates to an improved enzymic diagnostic assay to detect carcinoma by measuring various lysophospholipids, including lysophosphatidic acid (LPA), in a patient. In a preferred embodiment, this assay measures the human plasma level of LPA in an automated format with a minimal number of reagents and with reduced incubation periods. The present invention also comprises several addnl. tech. improvements to the current LPA assays disclosed in the prior art.

L4 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:480634 CAPLUS
DOCUMENT NUMBER: 135:43112
TITLE: Disease conditions by measuring lysophosphatidic acid
INVENTOR(S): Small, Christopher L.; Parrott, Jeff A.; Xu, Liang Shong
PATENT ASSIGNEE(S): Ataigrin Technologies, Inc., USA
SOURCE: U.S., 15 pp., Cont.-in-part of U.S. 6,248,553.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6255063	B1	20010703	US 1999-314780	19990519 <--
US 6248553	B1	20010619	US 1998-176813	19981022 <--
US 20020004213	A1	20020110	US 2001-897469	20010702 <--

PRIORITY APPLN. INFO.: US 1998-176813 A2 19981022
US 1999-314780 A1 19990519

AB The present invention is an enzymic method and diagnostic kits for detecting and quantifying the presence of one or more lysophospholipids in a sample of bodily fluid taken from a test subject. The method uses enzymes in a two step assay and may be used to detect disease conditions associated with altered levels of lysophospholipids and to correlate such conditions with altered levels of lysophospholipids.
REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:368605 CAPLUS
DOCUMENT NUMBER: 133:27360
TITLE: Recombinant human lysophosphatidic acid phosphatase and lysophosphatidic acid assay
INVENTOR(S): Takenawa, Tadaomi; Hiroyama, Masami; Kishimoto, Tatsuya; Yamaguchi, Masahiro; Toyosato, Mitsuyoshi; Mizuno, Kouji
PATENT ASSIGNEE(S): Azwell Inc., Japan
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000031275	A1	20000602	WO 1999-JP4509	19990823 <--
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1050584	A1	20001108	EP 1999-938570	19990823 <--
EP 1050584	B1	20061018		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6472193	B1	20021029	US 2000-600588	20000911 <--
US 20030104600	A1	20030605	US 2002-213100	20020807 <--
US 7109012	B2	20060919		

PRIORITY APPLN. INFO.:	JP 1998-329866	A	19981119
	WO 1999-JP4509	W	19990823
	US 2000-600588	A3	20000911

AB A recombinant human lysophosphatidic acid (LPA) phosphatase being capable of specifically hydrolyzing LPA; a method for assaying LPA by using the enzyme; and a measurement kit appropriate for this method, are disclosed. A cDNA encoding the LPA phosphatase; a method and compns. for producing LPA phosphatase including an expression vector and a transformant; are also claimed. Antibodies to the enzyme, antisense DNA or RNA, and primers and probes hybridizable to the LPAP gene are also claimed. A cDNA encoding lysophosphatidic acid (LPA) phosphatase (LPAP) was cloned from human. The amino acid sequence deduced from the cDNA encoding LPAP had 421 residues including a putative signal peptide and was homologous to acid phosphatase, especially at the active site. Human LPAP also had 28.5% amino acid identity to human prostatic acid phosphatase. GST-LPAP fusion proteins expressed in E. coli showed similar LPA phosphatase activity with or without the putative signal peptide. A method and reagents for assaying LPA by using the enzyme was developed to detect LPA specifically without detecting other phospholipids like PA, phosphatidyl ethanolamine (LPE), and phosphatidyl choline (LPC). The method and compns. of this invention may be useful in clarifying the LPA metabolic pathway and diagnosing and treating various diseases in which LPA participates.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2000:227676 CAPLUS
DOCUMENT NUMBER:	132:250004
TITLE:	Ligand presenting assembly (LPA), method of preparation and uses thereof
INVENTOR(S):	Holm, Arne; Jorgensen, Rikke Malene; Ostergaard, Soren; Theisen, Michael
PATENT ASSIGNEE(S):	Statens Serum Institut, Den.
SOURCE:	PCT Int. Appl., 100 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018791	A1	20000406	WO 1999-DK510	19990929 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,				

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            IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
            MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
            SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
            DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
            CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9960783          A     20000417    AU 1999-60783          19990929 <--
     EP 1117677          A1    20010725    EP 1999-947256         19990929 <--
     EP 1117677          B1    20031112
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, IE, SI, LT,
           LV, FI, RO
     AT 254137           T     20031115    AT 1999-947256         19990929 <--
     US 20040086949      A1    20040506    US 2003-724233         20031201
PRIORITY APPLN. INFO.:                      DK 1998-1233        A  19980929
                                            US 1999-408578      B1 19990929
                                            WO 1999-DK510       W  19990929
OTHER SOURCE(S):         MARPAT 132:250004
AB   The present invention relates to a method for preparing a Ligand Presenting
     Assembly (LPA), an LPA, an immunol. composition and a vaccine.  The N-terminal
     of LPA is coupled to an achiral di, tri, or tetra-carboxylic acid so as to
     provide a construct having a ring structure.  The invention further
     relates to a method for generating antibodies, a kit for use in
     diagnosis and use of an LPA for preparing a pharmaceutical composition
REFERENCE COUNT:         7     THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4   ANSWER 11 OF 11  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        1998:532381  CAPLUS
DOCUMENT NUMBER:         129:272557
ORIGINAL REFERENCE NO.:  129:55505a,55508a
TITLE:                   The development of rapid method for LpA-I by
                         turbidimetric immunoassay
AUTHOR(S):               Ishizuka, Masahiro; Takeda, Naokuni; Kaneko, Takashi;
                         Kondo, Kazuo; Kidou, Toshimi; Itakura, Hiroshige
CORPORATE SOURCE:        Dep. Medical Sci., Cosmo Res. Inst., Japan
SOURCE:                  Igaku to Yakugaku (1998), 39(5), 1041-1046
                         CODEN: IGYAEI; ISSN: 0389-3898
PUBLISHER:               Shizen Kagakusha
DOCUMENT TYPE:           Journal
LANGUAGE:                Japanese
AB   A method and kit were developed for determining lipoproteins containing
     only apoA-I (LpA-I).  The method involves addition of surfactant
     and anti-apoA-II antibody to the sample (blood serum or plasma),
     incubation, and centrifugal separation of LpA-I, then incubation with buffer
     solution and anti-apoA-I antibody and turbidimetric immunoassay with an
     automated analyzer.  The coefficient of variation ranged 0.71-1.10%.  This kit
     gave results that showed good correlation with those obtained by rocket
     immunoelectrophoresis.


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 NEWS  3  APR 03  CAS coverage of exemplified prophetic substances
                  enhanced
 NEWS  4  APR 07  STN is raising the limits on saved answers
 NEWS  5  APR 24  CA/CAplus now has more comprehensive patent assignee
                  information
 NEWS  6  APR 26  USPATFULL and USPAT2 enhanced with patent
                  assignment/reassignment information
 NEWS  7  APR 28  CAS patent authority coverage expanded
 NEWS  8  APR 28  ENCOMPLIT/ENCOMPLIT2 search fields enhanced
 NEWS  9  APR 28  Limits doubled for structure searching in CAS
                  REGISTRY
 NEWS 10  MAY 08  STN Express, Version 8.4, now available
 NEWS 11  MAY 11  STN on the Web enhanced
 NEWS 12  MAY 11  BEILSTEIN substance information now available on
                  STN Easy
 NEWS 13  MAY 14  DGENE, PCTGEN and USGENE enhanced with increased
                  limits for exact sequence match searches and
                  introduction of free HIT display format
 NEWS 14  MAY 15  INPADOCDB and INPAFAMDB enhanced with Chinese legal
                  status data
 NEWS 15  MAY 28  CAS databases on STN enhanced with NANO super role in
                  records back to 1992
 NEWS 16  JUN 01  CAS REGISTRY Source of Registration (SR) searching
                  enhanced on STN
 NEWS 17  JUN 26  NUTRACEUT and PHARMAML no longer updated

 NEWS 18  JUN 29  IMSCOPROFILE now reloaded monthly

 NEWS 19  JUN 29  EPFULL adds SLART to AB, MCLM, and TI fields

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              AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

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                                                         ENTRY    SESSION
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FULL ESTIMATED COST 0.22 0.22

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FILE 'BIOSIS' ENTERED AT 09:34:27 ON 30 JUN 2009

FILE 'CAPLUS' ENTERED AT 09:34:27 ON 30 JUN 2009
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FILE 'EMBASE' ENTERED AT 09:34:27 ON 30 JUN 2009

=> S ((EDG Receptor) OR (LPA1 Receptor)) (S) Kidney AND Expression
L1 3 ((EDG RECEPTOR) OR (LPA1 RECEPTOR)) (S) KIDNEY AND EXPRESSION

=> Dupe Rem L1
DUPE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> Dup Rem L1
PROCESSING COMPLETED FOR L1
L2 3 DUP REM L1 (0 DUPLICATES REMOVED)
ANSWERS '1-3' FROM FILE CAPLUS

=> D Ibib abs L2 1-3

L2 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2007:1453935 CAPLUS
DOCUMENT NUMBER: 148:535409
TITLE: LPA1 receptor activation promotes renal interstitial fibrosis
AUTHOR(S): Pradere, Jean-Philippe; Klein, Julie; Gres, Sandra; Guigne, Charlotte; Neau, Eric; Valet, Philippe; Calise, Denis; Chun, Jerold; Bascands, Jean-Loup; Saulnier-Blache, Jean-Sebastien; Schanstra, Joost P.
CORPORATE SOURCE: Inserm, U858/I2MR, Department of Metabolism and Obesity, Team 3, Institut Louis Bugnard, Toulouse, Fr.
SOURCE: Journal of the American Society of Nephrology (2007), 18(12), 3110-3118
CODEN: JASNEU; ISSN: 1046-6673
PUBLISHER: American Society of Nephrology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tubulointerstitial fibrosis in chronic renal disease is strongly associated with progressive loss of renal function. We studied the potential involvement of lysophosphatidic acid (LPA), a growth factor-like phospholipid, and its receptors LPA1-4 in the development of tubulointerstitial fibrosis (TIF). Renal fibrosis was induced in mice by unilateral ureteral obstruction (UUO) for up to 8 d, and kidney explants were prepared from the distal poles to measure LPA release into conditioned media. After obstruction, the extracellular release of LPA increased approx. 3-fold. Real-time reverse transcription PCR (RT-PCR) anal. demonstrated significant upregulation in the expression of the LPA1 receptor subtype, downregulation of LPA3, and no change of LPA2 or LPA4. TIF was significantly attenuated in LPA1 (-/-) mice compared to wild-type littermates, as measured by expression of collagen III, α-smooth muscle actin (α-SMA), and F4/80. Furthermore,

treatment of wild-type mice with the LPA1 antagonist Ki16425 similarly reduced fibrosis and significantly attenuated renal expression of the profibrotic cytokines connective tissue growth factor (CTGF) and transforming growth factor β (TGFβ). In vitro, LPA induced a rapid, dose-dependent increase in CTGF expression that was inhibited by Ki16425. In conclusion, LPA, likely acting through LPA1, is involved in obstruction-induced TIF. Therefore, the LPA1 receptor might be a pharmaceutical target to treat renal fibrosis.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1075963 CAPLUS
DOCUMENT NUMBER: 142:20821
TITLE: Cell density-dependent expression of EDG family receptors and mesangial cell proliferation: Role in lysophosphatidic acid-mediated cell growth
AUTHOR(S): Xing, Yiding; Ganji, Shobha H.; Noh, Jung W.; Kamanna, Vaijinath S.
CORPORATE SOURCE: Medical Research Service, Department of Veterans Affairs Healthcare System, Long Beach, 90822, USA
SOURCE: American Journal of Physiology (2004), 287(6, Pt. 2), F1250-F1257
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lysophosphatidic acid (LPA), a major member of the bioactive lysophospholipids in serum, possesses diverse physiol. activities including cell proliferation. Recently, three endothelial differentiation gene (EDG) family receptors, including EDG-2 (LPA1), EDG-4 (LPA2), and EDG-7 (LPA3), have been identified as LPA receptors. The role of LPA and their receptors in mesangial cell physiol. is not clearly understood. This study examined the expression profile of EDG receptors as a function of cell d. and the participation of EDG receptors in human mesangial cell proliferation by LPA. We showed that mesangial cells express all three EDG family LPA receptors in a cell d.-dependent manner. EDG-7 maximally expressed at sparse cell d. and minimally expressed in dense cell population. The EDG-2 expression pattern was opposite to the EDG-7. No changes in EDG-4 expression as a function of cell d. were noted. DNA synthetic rate was greater in sparse cell d. compared with dense cell population and followed a similar pattern with EDG-7 expression. Comparative studies in sparse and dense cell d. indicated that EDG-7 was pos. associated, whereas EDG-2 was neg. associated with cell proliferation rate. LPA induced mesangial cell proliferation by 1.5- to 3.5-fold. Dioctanoylglycerol pyrophosphate, an antagonist for EDG-7, almost completely inhibited mesangial cell proliferation induced by LPA. We suggest that EDG-7 regulates LPA-mediated mesangial cell proliferation. Addnl., these data suggest that EDG-7 and EDG-2 LPA receptors play a diverse role as proliferative and antiproliferative, resp., in mesangial cells. Regulation of EDG family receptors may be importantly linked to mesangial cell-proliferative processes.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:212940 CAPLUS
DOCUMENT NUMBER: 139:1403
TITLE: Pericyte-specific expression of RGS5: implications for PDGF and EDG receptor signaling during vascular maturation

AUTHOR(S): Cho, Hyeseon; Kozasa, Tohru; Bondjers, Cecilia; Betsholtz, Christer; Kehrl, John H.
CORPORATE SOURCE: National Institute of Allergy and Infectious Diseases, Lab. of Immunoregulation, National Institute of Allergy and Infectious Diseases, Bethesda, MD, 20892-1876, USA
SOURCE: FASEB Journal (2003), 17(3), 440-442, 10.1096/fj.02-0340fje
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB RGS proteins finely tune heterotrimeric G-protein signaling. Implying the need for such fine-tuning in the developing vascular system, in situ hybridization revealed a striking and extensive expression pattern of Rgs5 in the arterial walls of E12.5-E17.5 mouse embryos. The distribution and location of the Rgs5-pos. cells typified that of pericytes and strikingly overlapped the known expression pattern of platelet-derived growth factor receptor (PDGFR)-β. Both E14.5 PDGFR-β- and platelet-derived growth factor (PDGF)-B-deficient mice exhibited markedly reduced levels of Rgs5 in their vascular plexa and small arteries. This likely reflects the loss of pericytes in the mutant mice. RGS5 acts as a potent GTPase activating protein for Giα and Gqα and it attenuated angiotensin II-, endothelin-1-, sphingosine-1-phosphate-, and PDGF-induced ERK-2 phosphorylation. Together these results indicate that RGS5 exerts control over PDGFR-β and GPCR-mediated signaling pathways active during fetal vascular maturation.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FULL ESTIMATED COST	27.15	27.37

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                     ENTRY    SESSION
CA SUBSCRIBER PRICE                                  -2.46      -2.46

=> S (Mesangial cells) (P) ((EDG receptor) OR (LPA receptor))
L3          12 (MESANGIAL CELLS) (P) ((EDG RECEPTOR) OR (LPA RECEPTOR))

=> Dup REM L3
PROCESSING COMPLETED FOR L3
L4             4 DUP REM L3 (8 DUPLICATES REMOVED)
                 ANSWERS '1-3' FROM FILE MEDLINE
                 ANSWER '4' FROM FILE EMBASE

=> D Ibib ABS L4 1-4

L4   ANSWER 1 OF 4     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    2004550101     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 15292052
TITLE:               Cell density-dependent expression of EDG family receptors
                     and mesangial cell proliferation: role in lysophosphatidic
                     acid-mediated cell growth.
AUTHOR:              Xing Yiding; Ganji Shobha H; Noh Jung W; Kamanna Vaijinath
                     S
CORPORATE SOURCE:    Medical Research Service, Department of Veterans Affairs
                     Healthcare System, 5901 East Seventh St., Long Beach, CA
                     90822, USA.
SOURCE:              American journal of physiology. Renal physiology, (2004
                     Dec) Vol. 287, No. 6, pp. F1250-7.  Electronic Publication:
                     2004-08-03.
                     Journal code: 100901990. ISSN: 0363-6127.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
                     (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200501
ENTRY DATE:          Entered STN: 4 Nov 2004
                     Last Updated on STN: 4 Jan 2005
                     Entered Medline: 3 Jan 2005
AB   Lysophosphatidic acid (LPA), a major member of the bioactive
     lysophospholipids in serum, possesses diverse physiological activities
     including cell proliferation.  Recently, three endothelial differentiation
     gene (EDG) family receptors, including EDG-2 (LPA1), EDG-4 (LPA2), and
     EDG-7 (LPA3), have been identified as LPA receptors.
     The role of LPA and their receptors in mesangial cell physiology is not
     clearly understood.  This study examined the expression profile of
     EDG receptors as a function of cell density and the
     participation of EDG receptors in human mesangial cell
     proliferation by LPA.  We showed that mesangial cells
     express all three EDG family LPA receptors in a cell
     density-dependent manner.  EDG-7 maximally expressed at sparse cell
     density and minimally expressed in dense cell population.  The EDG-2
     expression pattern was opposite to the EDG-7.  No changes in EDG-4
     expression as a function of cell density were noted.  DNA synthetic rate
     was greater in sparse cell density compared with dense cell population and
     followed a similar pattern with EDG-7 expression.  Comparative studies in
     sparse and dense cell density indicated that EDG-7 was positively
     associated, whereas EDG-2 was negatively associated with cell
     proliferation rate.  LPA induced mesangial cell proliferation by 1.5- to
     3.5-fold.  Dioctanoylglycerol pyrophosphate, an antagonist for EDG-7,
     almost completely inhibited mesangial cell proliferation induced by LPA.
     We suggest that EDG-7 regulates LPA-mediated mesangial cell proliferation.
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Additionally, these data suggest that EDG-7 and EDG-2 LPA receptors play a diverse role as proliferative and antiproliferative, respectively, in mesangial cells. Regulation of EDG family receptors may be importantly linked to mesangial cell-proliferative processes.

L4 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002129834 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11829737
TITLE: Role of Rac and Cdc42 in lysophosphatidic acid-mediated cyclo-oxygenase-2 gene expression.
AUTHOR: Hahn Angelika; Barth Holger; Kress Michaela; Mertens Peter R; Goppelt-Struebe Margarete
CORPORATE SOURCE: Medizinische Klinik IV, Universitat Erlangen-Nurnberg, Loschgestr. 8, D-91054 Erlangen, Germany.
SOURCE: The Biochemical journal, (2002 Feb 15) Vol. 362, No. Pt 1, pp. 33-40.
Journal code: 2984726R. ISSN: 0264-6021.
Report No.: NLM-PMC1222357.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 28 Feb 2002
Last Updated on STN: 24 Mar 2002
Entered Medline: 22 Mar 2002

AB The role of Rho proteins in lysophosphatidic acid (LPA)-mediated induction of cyclo-oxygenase-2 (Cox-2) was investigated in renal mesangial cells. Previous studies had shown that toxin B, an inhibitor of Rho, Rac and Cdc42, suppressed Cox-2 induction. A role for RhoA in pertussis toxin-sensitive LPA signalling was excluded with C3 transferase from Clostridium limosum, used as the fusion toxin C2IN-C3 (where C2IN is part of the C2I toxin of C. botulinum). Incubation of the cells with C2IN-C3 disrupted cytosolic actin stress fibres, but had no effect on Cox-2 induction. Similarly, activation of p42/44 mitogen-activated protein kinase (MAP kinase), an upstream step in Cox-2 induction, was inhibited by toxin B, but not affected by C2IN-C3. Upon treatment with toxin B, focal adhesion kinase and paxillin were dephosphorylated at tyrosine residues and the actin cytoskeleton was completely destroyed. An intact cytoskeleton, however, was not required for p42/44 MAP-kinase activation or Cox-2 induction, as shown by the actin-depolymerizing agent cytochalasin D. Toxin B did not influence functionality of LPA receptors, because G(i)-mediated Ca(2+) release from intracellular stores remained unchanged. Within 1 h, toxin B inactivated and translocated RhoA and Cdc42 to the cellular membranes. Within the same time frame, monoglucosylated Rac1 was degraded. Direct stimulation of Rho proteins by cytotoxic necrotizing factor type 1 (CNF1) induced Cox-2 expression, which was sensitive to inhibition of the MAP-kinase pathway by PD98059, but not to an inhibitor of RhoA kinase. By exclusion of RhoA and non-specific cytoskeletal effects, the results in the present study indicate an important role for Rac and/or Cdc42 in pertussis toxin-sensitive LPA-mediated Cox-2 induction.

L4 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999189185 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10087253
TITLE: Lysophosphatidic acid and mesangial cells: implications for renal diseases.
AUTHOR: Inoue C N; Epstein M; Forster H G; Hotta O; Kondo Y; Iinuma K

CORPORATE SOURCE: Department of Pediatrics, Tohoku University School of Medicine, 1-1 Seiryo-machi, Sendai 980-8574, Japan.
SOURCE: Clinical science (London, England : 1979), (1999 Apr) Vol. 96, No. 4, pp. 431-6. Ref: 40
Journal code: 7905731. ISSN: 0143-5221.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 18 Jun 1999
Last Updated on STN: 18 Jun 1999
Entered Medline: 10 Jun 1999

AB The last decade has witnessed a phenomenal increase in our understanding of the biological role of lysophosphatidic acid (LPA) and has led to an appreciation of this critical serum-derived growth factor released from platelets. We herein summarize recent observations that collectively support the hypothesis that LPA may play a key role in the pathogenesis of initiation and progression of proliferative glomerulonephritis. LPA synergistically stimulates mesangial cell proliferation in combination with platelet-derived growth factor in primary culture. The mechanism of co-mitogenesis is likely to be mediated by the prolonged activation of mitogen-activated protein kinase which is stimulated by platelet-derived growth factor and LPA through different mechanisms. LPA contracts cultured mesangial cells and has properties in common with other pressor molecules including mobilization of intracellular Ca2+ and promotion of Ca2+ entry through dihydropyridine-sensitive calcium channels. LPA receptor mRNA has been identified in isolated glomeruli dissected from renal biopsy samples of patients with IgA nephropathy. All of these facts have led us to postulate that LPA is produced within glomeruli and that LPA's mitogenic as well as haemodynamic action contribute to the pathological process of mesangial proliferative glomerulonephritis. The possible production of LPA as an autocrine factor from mesangial cells themselves has also been discussed.

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ACCESSION NUMBER: 2004493416 EMBASE
TITLE: Cell density-dependent expression of EDG family receptors and mesangial cell proliferation: Role in lysophosphatidic acid-mediated cell growth.
AUTHOR: Kamanna, Vaijinath S. (correspondence)
CORPORATE SOURCE: Medical Research Service (151), Dept. of Vet. Aff. Healthcare System, 5901 East Seventh St., Long Beach, CA 90822, United States. vaijinath.Kamanna@med.va.gov
AUTHOR: Xing, Yiding; Ganji, Shobha H.; Noh, Jung W.
SOURCE: American Journal of Physiology - Renal Physiology, (Dec 2004) Vol. 287, No. 6 56-6, pp. F1250-F1257.
Refs: 47
ISSN: 0363-6127 CODEN: AJPPFK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 2004
Last Updated on STN: 9 Dec 2004

AB Lysophosphatidic acid (LPA), a major member of the bioactive lysophospholipids in serum, possesses diverse physiological activities

including cell proliferation. Recently, three endothelial differentiation gene (EDG) family receptors, including EDG-2 (LPA1), EDG-4 (LPA2), and EDG-7 (LPA3), have been identified as LPA receptors. The role of LPA and their receptors in mesangial cell physiology is not clearly understood. This study examined the expression profile of EDG receptors as a function of cell density and the participation of EDG receptors in human mesangial cell proliferation by LPA. We showed that mesangial cells express all three EDG family LPA receptors in a cell density-dependent manner. EDG-7 maximally expressed at sparse cell density and minimally expressed in dense cell population. The EDG-2 expression pattern was opposite to the EDG-7. No changes in EDG-4 expression as a function of cell density were noted. DNA synthetic rate was greater in sparse cell density compared with dense cell population and followed a similar pattern with EDG-7 expression. Comparative studies in sparse and dense cell density indicated that EDG-7 was positively associated, whereas EDG-2 was negatively associated with cell proliferation rate. LPA induced mesangial cell proliferation by 1.5- to 3.5-fold. Dioctanoylglycerol pyrophosphate, an antagonist for EDG-7, almost completely inhibited mesangial cell proliferation induced by LPA. We suggest that EDG-7 regulates LPA-mediated mesangial cell proliferation. Additionally, these data suggest that EDG-7 and EDG-2 LPA receptors play a diverse role as proliferative and antiproliferative, respectively, in mesangial cells. Regulation of EDG family receptors may be importantly linked to mesangial cell-proliferative processes.

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STN INTERNATIONAL SESSION SUSPENDED AT 09:42:04 ON 30 JUN 2009